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EFFECT ON WOUND HEALING OF BACTERICIDAL ULTRAVIOLET RADIATION FROM A SPECIAL* UNIT

EXPERIMENTAL STUDY

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Before utilizing a special ultraviolet irradiation unit for sterilizing the air in the operative region, with resultant exposure of the open wound, it seemed desirable to test the effect of radiation on wound healing in experimental animals.

As has been previously reported,[1] this unit consists of eight tubes 30 inches (75 cm.) long, mounted with two parallel tubes occupying the central part of each side of a square 5 feet (150 cm.) to the side. This square was mounted in a horizontal plane with its center approximately 4 feet 6 inches (137 cm.) above the operative site so as to place the center of each of the tubes about 5 feet from the incision. Over 80 per cent of the output of these radiation tubes is at 2,537 angstrom units. The intensity of radiation at the operative site, as measured by a photoelectric cell sensitive to this wavelength and calibrated with a bismuth-silver vacuum thermopile, is 28 to 30 microwatts per square centimeter.[2] A blond person exposed at this point for eighty minutes received no appreciable burn. There were some redness of the skin and a prickly sensation, which cleared within twenty-four hours. It has been demonstrated that with this intensity of radiation

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* Ultraviolet irradiation unit with over 80 per cent of its output at 2,537 angstrom units, giving an intensity of approximately 30 microwatts per square centimeter at the operative site.

1. Hart, D.: Operation Room Infections: Preliminary Report, Arch. Surg. **34**:874-896 (May) 1937.

2. Sharp, D. G.: A Quantitative Method of Determining the Lethal Effect of Ultraviolet Light on Bacteria Suspended in Air, J. Bact. **35**:589-599 (June) 1938.

and with exposure of less than five minutes the percentage of sterilization of a Petri dish of blood agar inoculated with Staphylococcus aureus haemolyticus [1] and other organisms [3] is between 95 and 100. It has also been shown that at this point this intensity of radiation reduces by over 95 per cent [1] the number of viable organisms dropping from the air.

MATERIAL AND METHOD

White rats were used for the shorter and dogs for the longer experiments. All operations were performed with the animals under ether anesthesia, and aseptic surgical technic was scrupulously followed except that in no case was any attempt made to keep sterile dressings in place after the operation. The incisions in rats for the first four groups of experiments were uniformly 3 to 4 cm. in length; those in dogs were made 12 to 15 cm. long, in order to allow greater exposure of the peritoneal surface. Closure was made in layers with interrupted sutures of black silk. The same technic was used for the control wounds except that they were exposed to the air with the same conditions under which the others were exposed to bactericidal radiation.

The following types of experiments were carried out:

1. Wounds were made in the abdominal wall down to the peritoneum and exposed as follows: in 3 rats, to bactericidal radiation for ten minutes; in 3 rats, to bactericidal radiation for twenty minutes; in 3 rats to bactericidal radiation for thirty minutes; and in 3 rats (controls), to air for ten, twenty and thirty minutes, respectively.

The animals were observed for three days after the operation.

2. Four incisions were made down to the peritoneum in the abdominal wall of each of 6 rats. One incision on each animal was used as a control, and the others were exposed for ten, twenty and thirty minutes respectively. A lead plate was used to protect the unexposed portion of each animal as well as the control wound. This group was observed for five days after the operation (fig. 1).

3. Incisions, one to either side of the midline, were made deep into the muscles of the back in each of 4 rats. Two wounds were exposed for ten minutes, two for twenty minutes and two for thirty minutes. Two were used as controls. This group was observed for five days after operation.

4. Bilateral incisions were made deep into the muscles on the posterior surfaces of the hindlegs of 8 rats. For each rat one incision was exposed to radiation and the other to the air for thirty minutes, the animal and the wound exposed to the air being protected from the radiation by a lead plate. This group was observed for six days.

After operation all wounds were observed for evidence of gross infection during periods varying from three to six days, as has been indicated. On the last day of observation the animals were killed, the wounds were grossly inspected, and blocks of tissue extending across the wound were taken for microscopic sections. From gross observation they were classified into four groups as follows:

A. Healing by first intention
B. Slight reaction
C. Moderate reaction
D. Gross suppuration

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3. Hart, D.; Devine, J. W., and Martin, D. W.: Bactericidal and Fungicidal Effect of Ultraviolet Radiation: Use of a Special Unit for Sterilizing the Air in the Operating Room, Arch. Surg., this issue, p. 806.

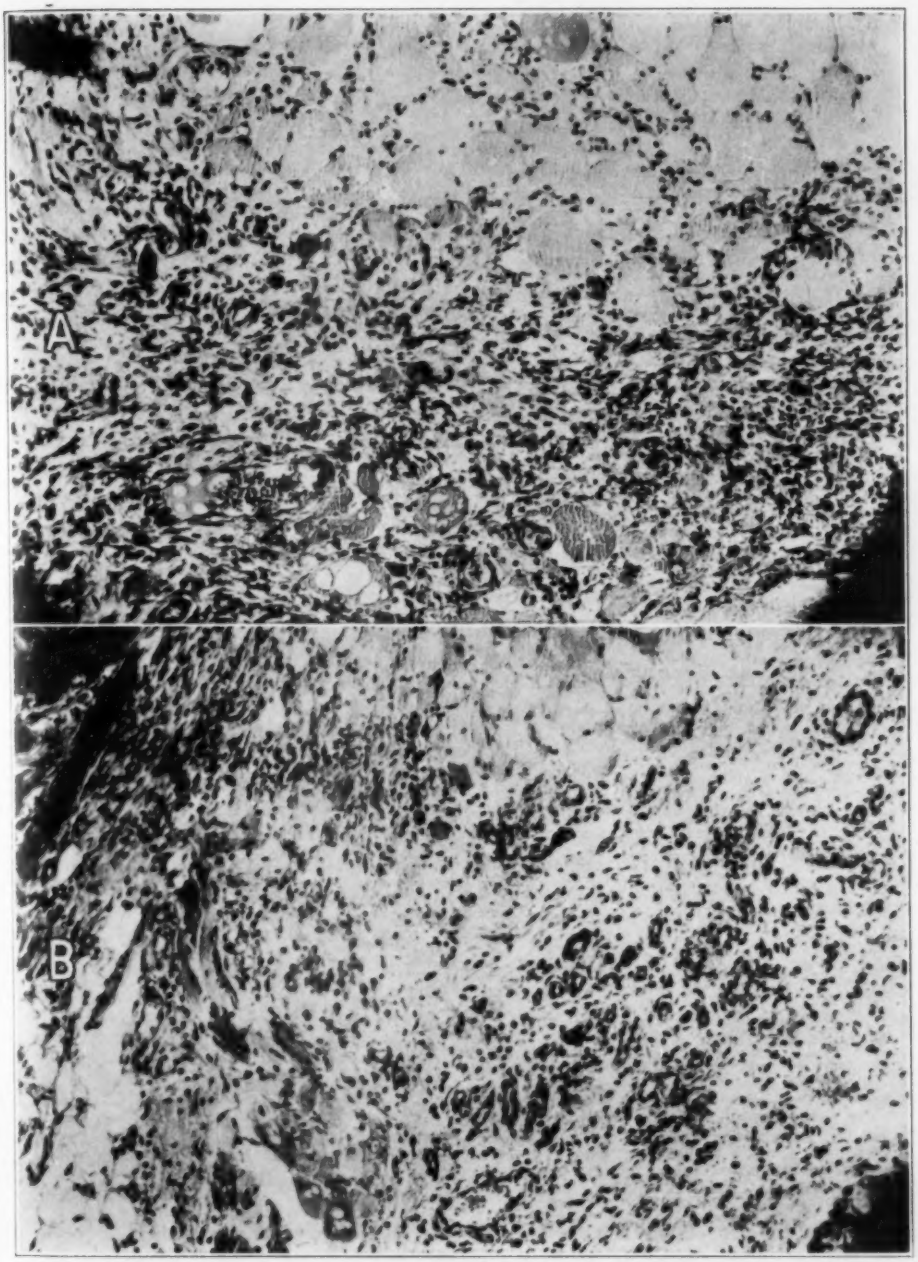

Fig. 1.—Comparison of the reaction in a wound (*A*) exposed to bactericidal radiation for thirty minutes with that in another wound (*B*) in the same animal, exposed to air for thirty minutes. Microscopic sections taken on the fifth day after exposure extend across the incision. From the study of a large number of sections it was our impression that there was less reaction in the wounds exposed to radiation. Certainly the reaction was no greater, and this is the point we wished to prove. It should be noted that in this case the control incision received some protection from the radiation, since it was in a room in which the air was being sterilized but was protected from the radiation by a sterile lead plate.

In all cases the microscopic observations as to the stage of healing and the wound reaction were classified into four groups, as follows:

A. Advanced primary healing
B. Primary healing in progress
C. Healing in progress but with some granulation tissue and inflammatory reaction
D. Slight healing with extensive inflammation

TABLE 1.—*Gross Appearance of Wounds*

Group*	Exposed to Bactericidal Radiation		Exposed to Air	
	Number of Wounds	Percentage of Irradiated Wounds in Each Group	Number of Wounds	Percentage of Control Wounds in Each Group
A	25	61.0	5	26.3
B	13	31.5	12	63.2
C	2	5.0	2	10.5
D	0	0	0	0
Died first day	1	2.5	0	0
Total	41	100.0	19	100.0

* In this table, groups A, B, C and D represent wounds classified as showing the following results: A, healing by first intention; B, slight reaction; C, moderate reaction; D, gross suppuration.

TABLE 2.—*Microscopic Study of Wounds*

Group*	Exposed to Bactericidal Radiation		Exposed to Air	
	Number of Wounds	Percentage	Number of Wounds	Percentage
A	19	46.4	4	21.0
B	15	36.6	13	68.4
C	5	12.2	1	5.3
D	1	2.4	1	5.3
Died first day	1	2.4	0	0
Total	41	100.0	19	100.0

* In this table, groups A, B, C and D represent wounds classified as showing the following results: A, advanced primary healing; B, primary healing in progress; C, healing in progress but with some granulation tissue and inflammatory reaction, and D, slight healing with extensive inflammation.

Since the four types of experiments were all similar and wound healing was about the same, the gross findings are tabulated in table 1, and the results of microscopic studies are recorded in table 2.

5. In order to test the effect of radiation on the peritoneum a long midline incision was made in each of 8 rats. In 6 the stomach, spleen and intestines were exposed to bactericidal radiation for thirty minutes. In the other 2 the same organs were exposed to the air for a similar period to serve as controls. The animals were killed seven days after the operation. There was no detectable difference in the number of adhesions, the amount of fluid or the appearance of the peritoneum.

6. In order to expose the peritoneum for a longer period than that during which a rat can be kept under anesthesia and to observe healing in the presence of soiling from an anastomosis in the gastrointestinal tract, 8 operations were carried out on 4 dogs. The results are shown in table 3, in which the gross appearance of the wound and of the peritoneal cavity are recorded. There was no evident difference in the amount of edema, the number of adhesions or the quantity of peritoneal fluid in the irradiated animals as compared with the

TABLE 3.—*Healing of Peritoneal Wounds in Dogs in the Presence of Anastomosis in the Gastrointestinal Tract*

Experiment	Dog	Operation	Peritoneum Exposed	Gross Appearance of Wound	Condition of Peritoneal Cavity Eight Days After Operation
1	T 1	Gastro-enterostomy	75 minutes	Slight reaction	Minimal adhesions around functioning gastroenterostomy
2	T 2	Gastro-enterostomy	80 minutes	Slight reaction	Minimal adhesions around functioning gastroenterostomy
3	T 3	Gastro-enterostomy	90 minutes	Healing by first intention	Few adhesions around functioning gastroenterostomy
4	T 4 Control	Gastro-enterostomy	Abdominal cavity left open without irradiation 80 minutes	Slight reaction	Minimal adhesions around functioning gastroenterostomy
5	T 1	Anastomosis of sigmoid (end to end) on 8th day after gastro-enterostomy had been done	90 minutes (week before, 75 minutes)	Wound broken down; fecal fistula	Fecal fistula; surprisingly few adhesions considering the pathologic picture
6	T 2	Same as experiment 5	80 minutes (week before, 80 minutes)	Healing by first intention	Relatively no adhesions or reaction
7	T 3	Same as experiment 5	90 minutes (week before, 90 minutes)	Healing by first intention	Relatively no adhesions or reaction
8	T 4 Control	Same as experiment 5	Abdominal cavity exposed to air without irradiation 90 min. (week before, 80 min.)	Slight reaction about wound	Essentially no difference from irradiated cavities

controls (fig. 2). In 1 case, after an end to end anastomosis of the colon, a fecal fistula developed. It was the opinion of the operator that irradiation was not responsible for the complication, and in this case there were remarkably few adhesions considering the leakage of intestinal contents.

7. In a number of dogs the brain or the spinal cord was exposed to radiation for sixty minutes, and in control animals these structures received a similar exposure to air. When the brain was exposed either to the air or to radiation there was no evident neurologic disturbance. When the spinal cord was exposed either to radiation or to air, certain dogs showed some weakness of the hindlegs, either as a result of poor surgical technic or owing to impairment of the stability

of the spinal column by the extent of the laminectomy. This weakness was thought to be related to the operative procedure rather than to the irradiation, since it affected the control dogs as well as the dogs exposed to radiation.

On both gross and microscopic examination of the brain (fig. 3) and the spinal cord (fig. 4) there was no demonstrable difference between the irradiated brain or spinal cord and the control. Further tests are being carried out on

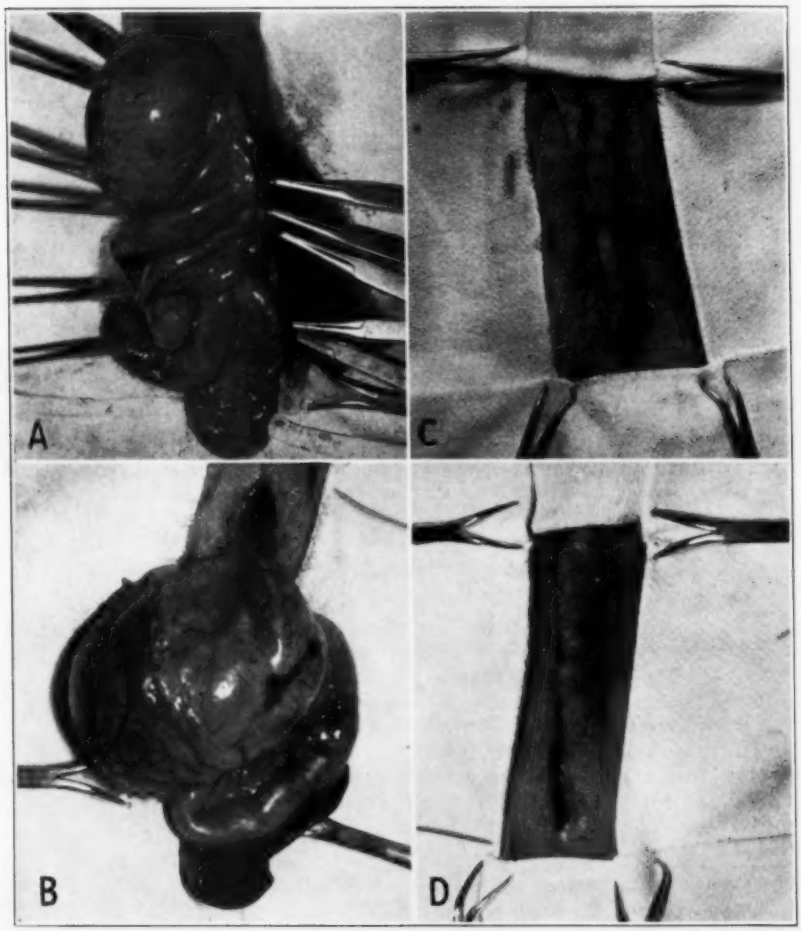

Fig. 2.—*A,* peritoneum (dog T2, table 3) exposed to radiation for eighty minutes. Gastroenterostomy was performed without the usual coverings of warm, moist pads. *B,* peritoneum (dog T4, table 3) exposed to air for eighty minutes as a control. Gastroenterostomy was performed without the usual coverings of warm, moist pads. In both the experimental and the control animal there was a notable absence of adhesions or other peritoneal reaction. *C,* abdominal incision (dog T2, table 3) exposed to bactericidal radiation for eighty minutes in addition to the time required for opening and closing. *D,* abdominal incision (dog T4, table 3) exposed to air for the same period, as a control. Healing of the abdominal incision was better in the animal exposed to radiation than in the control, although both are recorded as showing a slight reaction (table 3).

dogs by an investigator trained in neurosurgical technic, and the tissues are being studied by means of special stains.

Since these experiments were carried out, over 1,000 operations have been performed on patients, with no demonstrable ill effect on the skin, peritoneum, meninges or other tissue exposed in the wound.[4]

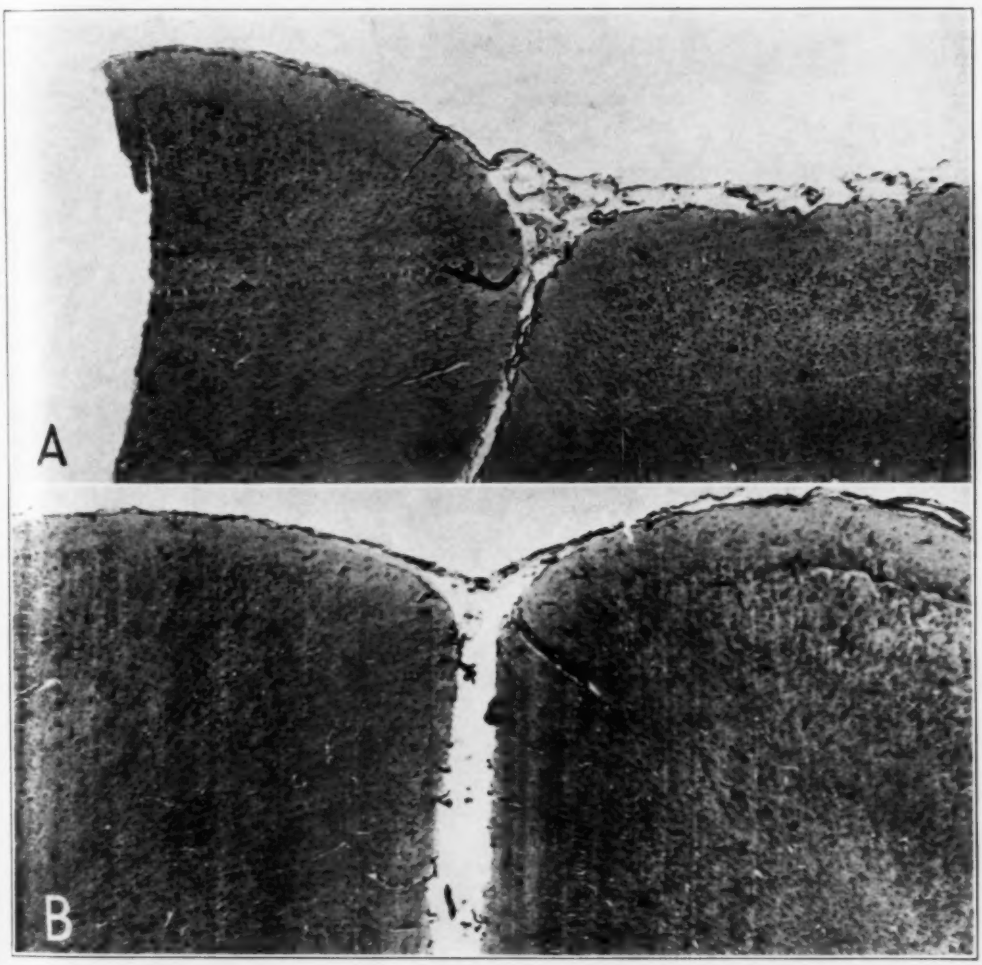

Fig. 3.—Photomicrographs of the brains of 2 dogs fourteen days after operation (hematoxylin and eosin stain). *A*, brain exposed to bactericidal radiation for sixty minutes. *B*, control specimen, exposed to air for sixty minutes. In both cases the brain was kept moist but was not otherwise protected. There was no appreciable difference between the irradiated brain and the control.

4. Hart, D.: Sterilization of the Air in the Operating Room by Bactericidal Radiant Energy: Results in Over Eight Hundred Operations, Arch. Surg. **37:**

(Footnote continued on next page)

No attempt is made to protect the skin or the wound beyond the precautions included in our usual operating room technic. This consists in covering the skin as soon as the incision is made, in avoiding undue exposure of the viscera or other denuded tissue and in keeping the exposed brain or spinal cord covered with warm, wet cotton. We have

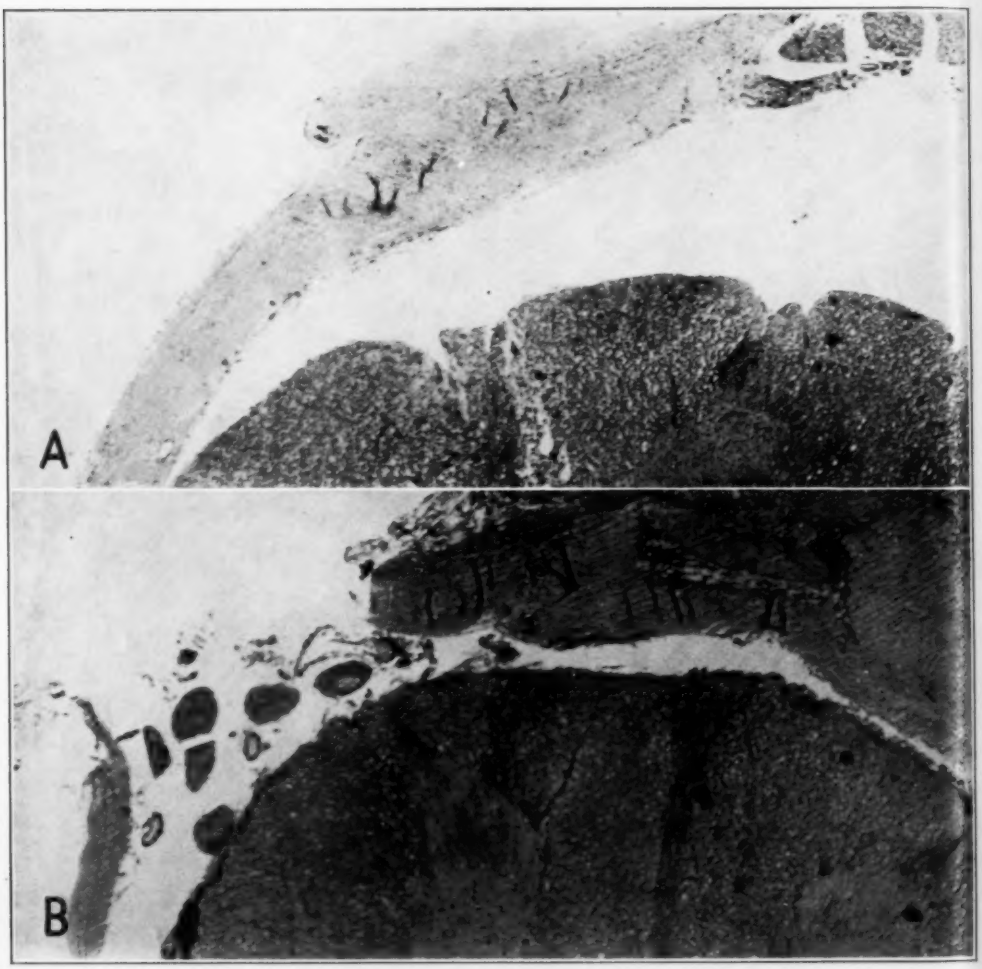

Fig. 4.—Photomicrographs of the spinal cords of 2 dogs fourteen days after operation (hematoxylin and eosin stain). A, spinal cord exposed to bactericidal radiation for sixty minutes. *B*, control specimen, exposed to air for sixty minutes. In both cases the spinal cord was kept moist but was not otherwise protected. There was no appreciable difference between the irradiated cord and the control.

956 (Dec.) 1938; Sterilization of the Air in the Operating Room with Bactericidal Radiation: Comparative Analysis of One Hundred and Thirty-Two Individual Stages of Extrapleural Thoracoplasties Performed With Radiation and One Hundred and Ten Stages Performed Without Radiation, J. Thoracic Surg. **7**: 525-535 (June) 1938.

avoided exposing the spinal cord for more than twenty to thirty minutes. It is seldom necessary to expose any part of a wound for a longer period. In such operations as radical mastectomy and repair of a large ventral hernia the tissues have been exposed for much longer periods without evident damage.

SUMMARY

Wounds in animals exposed for from ten to ninety minutes to bactericidal radiation as it is used to sterilize the air in the operative field healed as well as control wounds, if not better.

Exposure of the peritoneum to this intensity of radiation for from thirty to ninety minutes produced no damage demonstrable by adhesions, edema or increased fluid in the cavity.

Subsequent operations on over 1,000 patients with the wound exposed to an intensity of radiation at least as great as this have caused no demonstrable harm to the skin, peritoneum, meninges or other tissues exposed. The wounds heal with less reaction and less risk of infection, and there is less systemic reaction.

CONCLUSIONS

Bactericidal irradiation, which will render the air in the operative region almost free of viable organisms, offers little, if any, risk of damage to the patient if his eyes are protected and the usual precautions are taken to avoid prolonged and unnecessary exposure.

Healing is better in an irradiated wound than in one not irradiated, there being less danger of infection and less local and systemic reaction.

The slight inconvenience of protecting the eyes and skin of the operating room personnel is overbalanced by the greater security given the patient, particularly for extensive operative procedures performed during those times of the year and in those operating rooms in which there are a considerable number of pathogenic bacteria in the air.[5]

The irradiation units employed in this study were supplied by the Westinghouse Electric and Manufacturing Company.

5. Hart, D.: Pathogenic Bacteria in the Air of Operating Rooms: Their Widespread Distribution and the Methods of Control, Arch. Surg. **37**:521 (Oct.) 1938. Hart, D., and Schiebel, H. M.: Role of the Respiratory Tract in Contamination of Air: A Comparative Study, ibid. **38**:788 (April) 1939.

BACTERICIDAL AND FUNGICIDAL EFFECT OF ULTRAVIOLET RADIATION

USE OF A SPECIAL * UNIT FOR STERILIZING THE AIR IN THE OPERATING ROOM

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There are many reports in the literature dealing with the effect of ultraviolet radiation on bacteria. In an effort to kill the bacteria floating in the air of the occupied operating room we turned to such radiation, which is known to have strong bactericidal properties. (Wells [1] has been working on a similar problem, an attempt to control contamination of air from the standpoint of public health.) We have used cold tubes 30 inches (75 cm.) long, containing argon, neon and mercury. Over 80 per cent of the output of such tubes (which have already been described [2]) is at 2,537 angstrom units, and the apparatus offers the following advantages:

1. High output in the bactericidal range of the spectrum and low output in the erythemic range.

2. Negligible production of ozone, which is rarely detectable by odor even with as many as sixteen tubes burning in the operating room.

3. Negligible production of heat.

4. Low cost of the irradiation unit, which is made of high transmission glass instead of quartz.

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* Over 80 per cent of the output at 2,537 angstrom units, giving an intensity of approximately 30 microwatts per square centimeter at the point of exposure.

1. Wells, W. F., and Wells, M. W.: Air-Borne Infection, J. A. M. A. **107**:1698-1703 (Nov. 21) 1936; Air-Borne Infection: Sanitary Control, ibid. **107**: 1805-1809 (Nov. 28) 1936.

2. Sharp, D. G.: A Quantitative Method of Determining the Lethal Effect of Ultra-Violet Light on Bacteria Suspended in Air, J. Bact. **35**:589-599 (June) 1938.

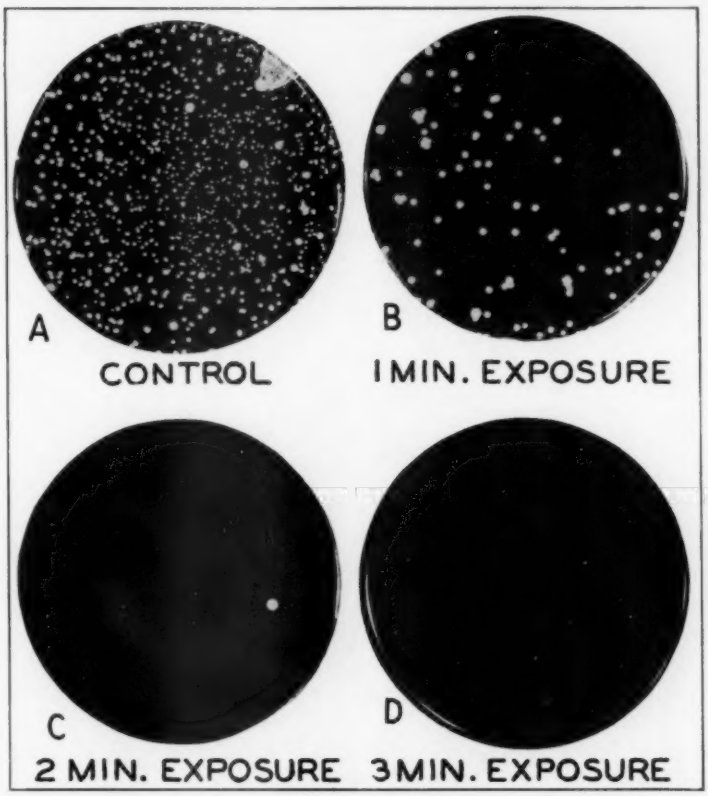

Fig. 1 (Staph. albus).—Photographs of one series of blood agar plates exposed to bactericidal radiation at a distance of 5 feet (150 cm.), from eight irradiation tubes each 30 inches (75 cm.) long. These tubes were arranged on a horizontal square 5 feet (150 cm.) to the side, with two parallel tubes occupying the central 30 inches (75 cm.) of each side. The center of the square was approximately 4.5 feet (135 cm.) above the Petri dish, so that the organisms were 5 feet (150 cm.) from the center of the individual tubes. Measurement of the intensity of the radiation at this point with a photoelectric cell sensitive to radiation at 2,537 angstrom units and calibrated with a bismuth-silver vacuum thermopile [2] showed it to be approximately 28 to 30 microwatts per square centimeter. Staph. albus is representative of organisms quickly killed by a given intensity of radiation. *A*, control plate sprayed with a dilute culture of Staph. albus; *B*, plate similarly prepared, photographed after irradiation for one minute; *C*, plate after irradiation for two minutes; *D*, plate after irradiation for three minutes. All plates were incubated for forty-eight hours at 37.5 C. before the colonies were counted and the photographs taken.

Staphylococcus citreus and Bacillus proteus showed about the same resistance (table 1).

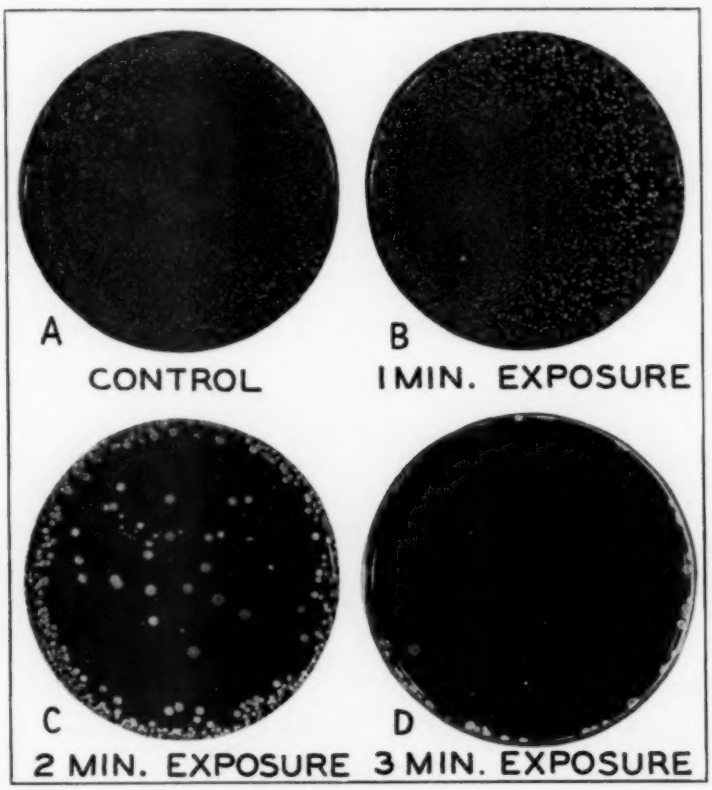

Fig. 2 (B. pyocyaneus).—Photographs of one series of blood agar plates exposed to bactericidal radiation under conditions identical with those given for figure 1. It should be noted that more colonies of this organism than of Staph. albus (fig. 1) survived a given period of exposure. This is probably accounted for partly by the increased density of the inoculation, but, in addition, B. pyocyaneus seemed to have a greater resistance. The organisms on the periphery of the plate were shaded from part of the radiation by the upright edge of the dish and survived longer than those not so shaded. *A*, control plate sprayed with a dilute culture of B. pyocyaneus; *B*, similarly treated plate after irradiation for one minute; *C*, plate after irradiation for two minutes; *D*, plate after irradiation for three minutes.

Bacillus coli and Streptococcus haemolyticus beta had about the same resistance (table 1).

5. Low operating cost (the estimated life of the tube is four thousand to five thousand hours, and from ten to sixteen tubes can be operated with as little current as is required by a 150 watt electric light bulb).

One of us (D. H.[3]) has already reported the effect on Staphylococcus aureus of radiation from eight such tubes at distances varying from 5 to 10 feet (150 to 300 cm.) and has shown its efficiency in reducing the number of viable bacteria floating in the air in the vicinity of the incision and sterile supplies. The widespread distribution of pathogenic bacteria in the air of the operating room has also been shown in a previous publication.[4]

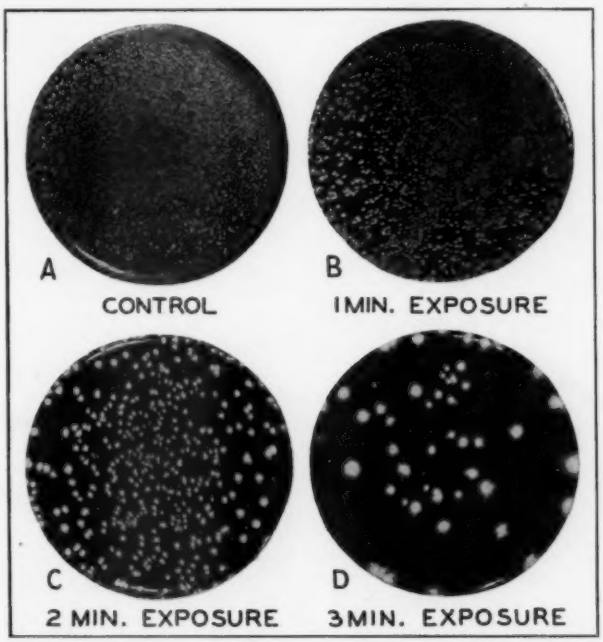

Fig. 3 (B. subtilis).—Photographs of one series of blood agar plates exposed as indicated for figure 1. This is representative of the most resistant of the bacteria tested. A similar picture was given by Friedländer's bacillus (Klebsiella pneumoniae, table 1). In contrast to the results shown in figures 1 and 2, a number of colonies in the central part of the plate, without any shading, survived an exposure of three minutes. The inoculation was fairly dense, and this probably played some part in the increased number of survivals. In addition, the resistance of the organism seemed to be greater. *A*, control plate sprayed with a dilute culture of B. subtilis; *B*, similarly prepared plate after irradiation for one minute; *C*, plate after irradiation for two minutes; *D*, plate after irradiation for three minutes.

3. Hart, D.: Operation Room Infections: Control of Air-Borne Pathogenic Organisms, with Particular Reference to the Use of Special Bactericidal Radiant Energy; Preliminary Report, Arch. Surg. **34**:874-896 (May) 1937.

4. Hart, D.: Pathogenic Bacteria in the Air of Operating Rooms: Their Widespread Distribution and Methods of Control, Arch. Surg. **37**:521 (Oct.) 1938.

This report makes no claim of discussing exhaustively the effect of ultraviolet radiation on bacteria. It is made to show the lethal effect produced with the particular irradiation unit used for this group of experiments on various bacteria and fungi at a distance of 5 feet (150 cm.) from each of the eight radiation tubes, that is, at the operative site as the tubes are mounted in the operating room.[3] At longer or shorter distances the intensity of radiation varies approximately inversely

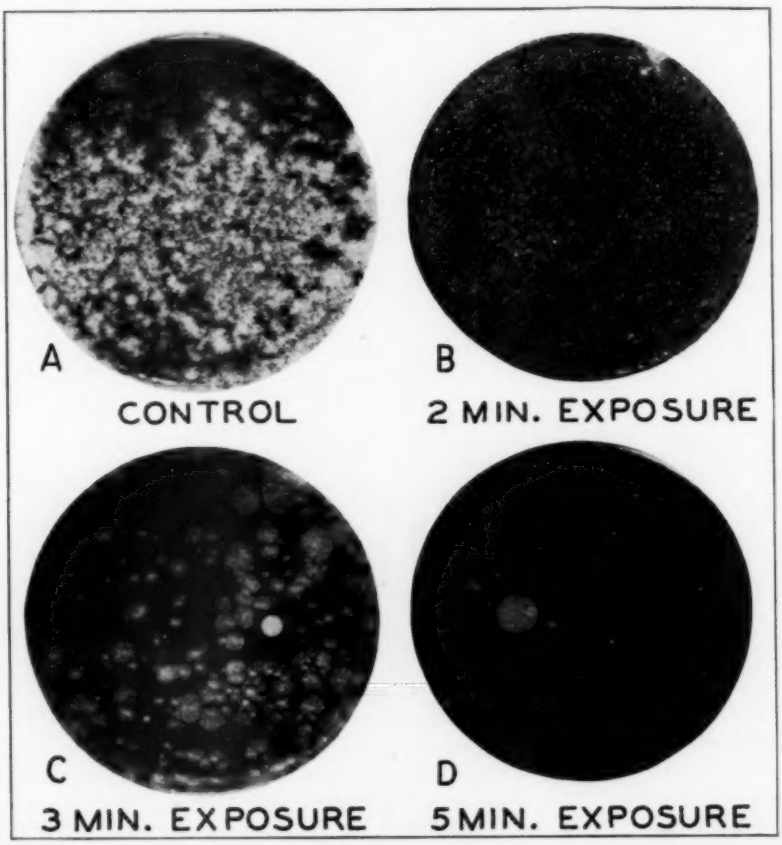

Fig. 4 (Mucor).—Photographs of a series of blood agar plates exposed as indicated in the descriptions of the foregoing illustrations. *A*, control plate; *B*, plate after irradiation for two minutes; *C*, plate after irradiation for three minutes; *D*, plate after irradiation for five minutes. Mucor and Monilia were the least resistant of the fungi tested (table 2).

as the square of the distance from the source of radiation and may be compensated by variations in the output of the unit. (Further studies are being carried on with the help of Mr. D. G. Sharp, their object being

the more accurate determination of the amount of energy from this irradiation unit required to kill various bacteria floating in the air.)

MATERIAL AND METHOD

Cultures of the bacteria listed in table 1 were prepared as follows: A fresh twenty-four hour broth culture was diluted 1:10,000 with sterile water, and the solution was placed in an atomizer. Twenty blood agar plates (p_H., 7.4) were

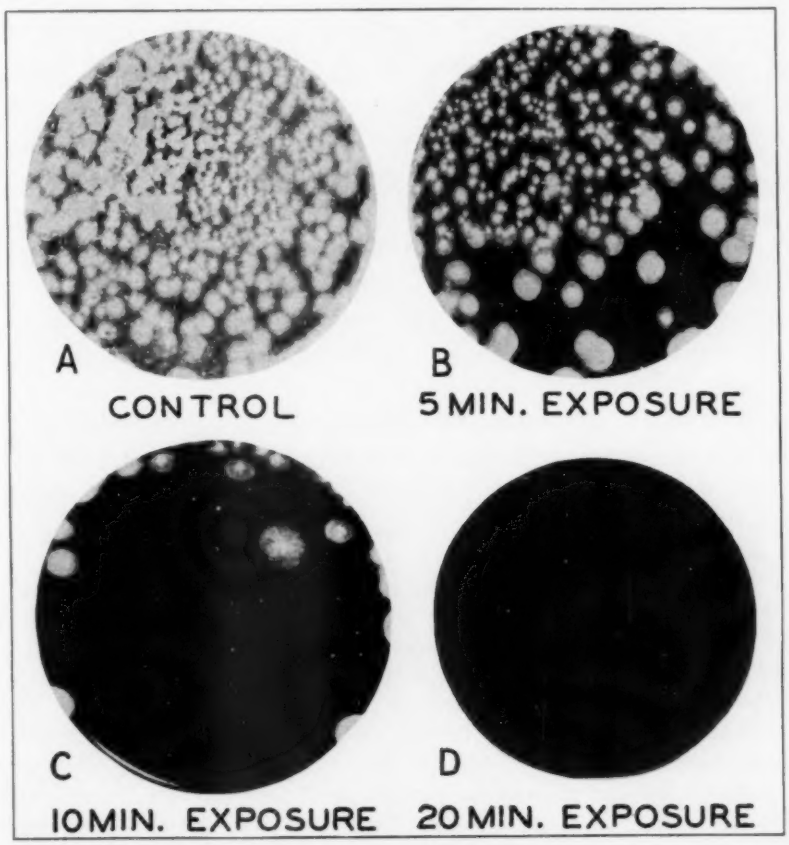

Fig. 5 (Geotrichum).—Photographs of a series of blood agar plates exposed as indicated in the descriptions of the foregoing illustrations. *A*, control plate; *B*, plate after irradiation for five minutes; *C*, plate after irradiation for ten minutes; *D*, plate after irradiation for twenty minutes. Some colonies of Dematium, Penicillium and Cladosporium survived an exposure of ten minutes, but all were killed by an exposure of twenty minutes (table 2). As in the case of the bacteria, the colonies at the periphery of the plate, which were shaded from part of the radiation by the upright edge of the Petri dish, survived longest.

sprayed at a distance of 12 inches (30 cm.) with each type of organism. Five of the twenty plates were used as controls to show the density of inoculation.

The remaining plates were exposed to radiation from a unit of eight tubes[5] (for arrangement of the tubes, see legend to figure 1) at a distance of 5 feet (150 cm.) from the individual tubes for periods of one, two and three minutes. This allowed five plates for each period of exposure. All plates were then incubated for forty-eight hours at 37.5 C.

The average number of colonies per Petri dish for the controls and for each period of exposure are shown in table 1. The values given in this table, particularly those designated by the word "innumerable," can be compared with photographs of a single control plate and a series of exposures of Staphylococcus albus (fig. 1), Bacillus pyocyaneus (fig. 2) and Bacillus subtilis (fig. 3).

It will be noted both in table 1 and in the photographs that there are variations in the susceptibility of different organisms. We do not wish to emphasize these variations or draw any conclusions until more accurately controlled experiments are completed, but we do wish to emphasize the fact that a large percentage of every type of bacteria tested were killed by relatively few minutes of exposure. From these and other tests we know that for this density of inoculation and with this intensity of radiation, sterilization reaches a level of over 95 per cent after three minutes of exposure. Some of the variations shown in the table may be dependent on the density of inoculation, but different organisms with the same density of inoculation still show variations in the time required for sterilization, indicating a difference in their resistance.

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5. In a previous publication[3] it has been shown that a blond person can be exposed to this intensity of radiation (approximately 28 to 30 microwatts per square centimeter of radiation at 2,537 angstrom units, this being over 80 per cent of the total radiation from the tubes) for eighty minutes without an appreciable burn. There are a prickly sensation and some redness of the skin, which clears within twenty-four hours. In over 1,000 operations, some performed with a much greater intensity of radiation, no patient has received an appreciable burn and no patient has had any complaint which could be ascribed to the irradiation (Hart, D.: Sterilization of the Air in the Operating Room by Bactericidal Radiant Energy: Results in Over Eight Hundred Operations, Arch. Surg. **37:** 956 [Dec.] 1938; Sterilization of the Air in the Operating Room with Bactericidal Radiation: Comparative Analysis of One Hundred and Thirty-Two Individual Stages of Extrapleural Thoracoplasties Performed with Radiation and One Hundred and Ten Stages Performed Without Radiation, J. Thoracic Surg. **7:**525-535 [June] 1938). Over 100 experiments on animals have shown that wounds exposed to this intensity of radiation for from ten to ninety minutes healed as well as those of the controls, if not better (Hart, D., and Sanger, P. W.: Effect on Wound Healing of Bactericidal Ultraviolet Radiation from a Special Unit: Experimental Study, Arch. Surg., this issue, p. 797).

Cultures of the fungi tested (table 2) were prepared as follows: A fresh transplant of each was made to a Sabouraud slant and allowed to grow at room temperature. When the growth covered the slant completely, sterile water was added to fill the tube and an emulsion was made. The resulting emulsion was

TABLE 1.—*Effect of Ultraviolet Radiation* on Various Bacteria*

Bacterium	Average Number of Colonies† per Plate			
	Control	1 Minute	2 Minutes	3 Minutes
Staph. albus	Innumerable	66	15	2
Staph. citreus	160	102	35	6
B. proteus	Innumerable	61	7	2
B. pyocyaneus	Innumerable	Innumerable	200	38
B. coli	Innumerable	Innumerable	Innumerable	8
Str. haemolyticus beta	Innumerable	98	53	12
B. subtilis	Innumerable	Innumerable	220	42
K. pneumoniae (Friedländer's bacillus)	Innumerable	110	100	19

* Over 80 per cent of the output was at 2,537 Å. The intensity of radiation was from 28 to 30 microwatts per square centimeter.

† The number of colonies surviving each period of exposure was somewhat increased by partial shading of the periphery of the plate by the upright edge of the Petri dish (figs. 1, 2 and 3).

TABLE 2.—*Effect of Ultraviolet Radiation* on Various Fungi*

Fungus	Average Number of Colonies† per Plate							
	Control	1 Min.	2 Min.	3 Min.	5 Min.	10 Min.	20 Min.	60 Min.
1. Monilia	Innumerable	200	150	45	0	0	0	0
2. Mucor	Innumerable	Innumerable	Innumerable	60	25	0	0	0
3. Geotrichum	Innumerable	Innumerable	Innumerable	Innumerable	180	20	0	0
4. Dematium	Innumerable	Innumerable	Innumerable	Innumerable	Innumerable	Innumerable	0	0
5. Penicillium	Innumerable	+	+	+	+	+	0	0
6. Cladosporium	Innumerable	+	+	+	+	+	0	0
7. Aspergillus	Innumerable	Innumerable	Innumerable	Innumerable	Innumerable	Innumerable	70	50

* Over 80 per cent of the output was at 2,537 Å. The intensity of radiation was from 28 to 30 microwatts per square centimeter.

† The number of colonies surviving each period of exposure was somewhat increased by partial shading of the periphery of the plate by the upright edge of the Petri dish (figs. 4, 5 and 6). The greater resistance of fungi as compared with bacteria may be accounted for in part by their tendency to form clumps which cannot be readily broken up. Aspergillus, which has a large amount of pigment and normally grows in the sunshine, was by far the most resistant fungus tested.

diluted 1:2,000 and was placed in an atomizer. Eight Sabouraud plates were sprayed with each emulsion at a distance of 12 inches (30 cm.). One plate was used as a control, and the remainder were exposed to the same intensity and spectral distribution of radiation as was used for the bacteria. Irradiation was

continued for one, two, three, five, ten, twenty and sixty minutes (except for Cladosporium and Penicillium, which were counted only after exposure for twenty and sixty minute periods, previous tests with these two organisms having shown that plates sprayed with them are not sterilized by an exposure of ten minutes).

The results are shown in table 2, which may be compared with the photographs of a single control and a series of exposures of Mucor (fig. 4), Geotrichum (fig. 5) and Aspergillus (fig. 6).

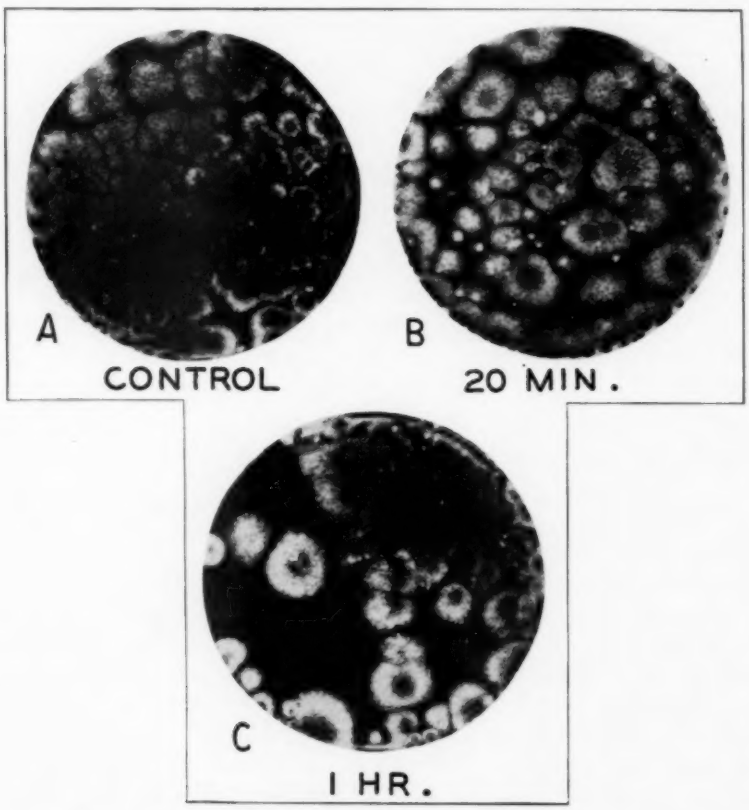

Fig. 6 (Aspergillus).—Photographs of a series of blood agar plates exposed as indicated in the descriptions of the foregoing illustrations. *A*, control plate; *B*, plate after irradiation for twenty minutes; *C*, plate after irradiation for one hour. This fungus, which normally grows in the sunshine, and contains a large amount of pigment, was the only one tested which was not killed by an exposure of twenty minutes. An exposure of sixty minutes had some effect, but many of the colonies survived.

SUMMARY

Various bacteria and fungi have been sprayed on culture plates and exposed to bactericidal radiation (over 80 per cent of the output of the irradiation unit being at 2,537 angstrom units [2]) at a distance of 5 feet

(150 cm.) from the center of the tubes. While the bacteria showed some variation in resistance, most of them were killed by an exposure of three minutes. The irradiation was also effective for killing fungi. Fungi were more resistant than the bacteria and varied widely in their susceptibility. Aspergillus (a nonpathogen), which grows in the sunshine and produces a large amount of pigment, was the most resistant; it was the only one which survived an exposure of twenty minutes, and some of its colonies survived an exposure of one hour. The tendency of fungi to grow in clumps may account in part for their greater resistance.

CONCLUSION

Special ultraviolet radiation (over 80 per cent of the output of the irradiation unit being at 2,537 angstrom units [2]) with low erythemic and high bactericidal properties, with a negligible production of ozone and heat and derived from a source which is relatively inexpensive for installation and operation, is highly efficient in killing many and possibly all bacteria and fungi at a distance of 5 feet (the intensity of radiation being 30 microwatts per square centimeter) and is a valuable contribution to the development of an aseptic surgical technic.

The Westinghouse Electric and Manufacturing Company contributed all the irradiation units used in this study.

TUMOR OF THE BRAIN AS A CAUSE OF DISORDERS OF THE AUTONOMIC NERVOUS SYSTEM

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MOSCOW, U. S. S. R.

Clinical studies and pathologic experiments have contributed to a broad investigation of the peripheral dystrophies associated with diseases of the brain.

Successive researches made in this domain (Schiff and Rokitansky;[1] Charcot;[2] Andral;[3] Arndt;[4] Mogilnitzky;[5] Burdenko;[6] Nikolajew;[7] Korst;[8] Cushing[9]) have laid the foundation for an original theory of the genesis of certain types of gastric and duodenal ulcer. This conception establishes a direct connection between the development of chronic ulcer and the destruction of the trophic centers. Experiments performed by Burdenko and Mogilnitzky,[10] Pigalew[11] and Skoblo[12] (from the laboratory directed by Speransky[13]) and consisting in infliction of various kinds of trauma on the region of the diencephalon have created a new basis for the aforementioned theory.

From the faculty clinic of the First Medical Institute, Prof. N. N. Burdenko, Director, and from the Department of Human Morphology of the A. M. Gorky All-Union Institute of Experimental Medicine, Prof. B. I. Lawrentjew, Director.

1. Schiff and Rokitansky, in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1926, vol. 3.

2. Charcot: Léçons, in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1926, vol. 4, p. 579.

3. Andral, G.: Clinique médicale, ou choix d'observations recuellies à l'Hôpital de la charité (clinique de M. Lerminier), ed. 3, Paris, Crochard & Cie, 1840, vol. 5, p. 200.

4. Arndt, R.: Deutsche med. Wchnschr. **14**:83, 1888.

5. Mogilnitzky, B. N.: Virchows Arch. f. path. Anat. **257**:109, 1925.

6. Burdenko, N.: Ztschr. f. d. ges. Neurol. u. Psychiat. **148**:343, 1933.

7. Nikolajew, cited by Burdenko.[6]

8. Korst, L.: J. sovrem. chir. **3**:607, 1928.

9. Cushing, H.: Surg., Gynec. & Obst. **55**:1, 1932.

10. Burdenko, N., and Mogilnitzky, B. N.: Ztschr. f. d. ges. Neurol. u. Psychiat. **103**:42, 1926.

11. Pigalew, I. A.: Ztschr. f. d. ges. exper. Med. **82**:617, 1932.

12. Skoblo, M. S.: Ztschr. f. d. ges. exper. Med. **73**:57, 1930.

13. Speransky, A. D.: Elementry postroenja teory mediziny, Moskow, Wiem, 1935.

As regards the pathologic picture presented by the autonomic nervous system in cases of peripheral dystrophy, Mogilnitzky, Sipovskiy [14] and also Zajewloschin and Rubinstein [15] have discovered phenomena of degeneration and irritation in the nervous elements of the solar plexus and of the cervical sympathetic ganglions in the presence of round ulcer, the alterations being mainly manifested in the solar plexus. The data obtained by Stöhr [16] and Rieder,[17] who have investigated the intramural autonomic nervous system (plexuses of Auerbach and Meissner) in the gastric wall in the presence of chronic ulcerous processes and found there a number of morphologic destructive alterations, may be used as additional evidence of the trophic origin of gastric and duodenal ulcer. Similar alterations in the intramural nervous system, as well as in the sympathetic ganglions associated with ulcerous processes of the intestine, have been detected by Wail. In the presence of some diseases associated with dystrophy, alterations in the central nervous system have also been found. Thus, in a number of cases of cerebral cachexia Shapiro [18] has discovered alterations (gliosis or neuronophagy) in the diencephalon. Stief [19] and also Peters [20] have observed degenerative alterations in the nuclei of the diencephalon in the presence of severe, exhausting diseases, such as progressive paralysis and cancerous cachexia. The data proving the existence of a close anatomic and functional connection between processes developed in the brain and processes developed in the peripheral autonomic nervous system led me to undertake a pathoanatomic study of the ganglions of the sympathetic trunk and the ganglions and trunks of the vagus nerve in cases of tumor of the brain. In the presence of a tumor of the brain the alterations of the cerebral tissue mainly involve the glia. The ganglionic elements in the close vicinity of the tumor exhibit considerable resistance. For instance, degenerative phenomena (disappearance of cells in the cortex) are detected only for a distance of some millimeters from the tumor. In all remaining regions the cells remain normal (Weber; [21] Casper [22]). Under the action of pressure the ganglionic cells near the tumor may change their form; they become flattened but keep the Nissl substance.

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14. Sipovskiy, P. W.: Arch. pat. anat. i patol. physiol. **1**:102, 1935.

15. Zajewloschin, M. N., and Rubinstein, B.: Arch. pat. anat. i patol. physiol. **1**: 97, 1935.

16. Stöhr, P., Jr.: Ztschr. f. Zellforsch. u. mikr. Anat. **16**:123, 1932.

17. Rieder, W.: Deutsche Ztschr. f. Chir. **244**:471, 1935.

18. Shapiro: Trudy I Moskovskogo Meditsinskogo Instituta, 1936, vol. 6.

19. Stief, cited by Josephi, in Hirsch, M.: Handbuch der innere Sekretion, Leipzig, Curt Kabitzsch, 1929.

20. Peters, G.: Ztschr. f. d. ges. Neurol. u. Psychiat. **154**:331, 1935.

21. Weber, cited by Casper.[22]

22. Casper, J.: Ztschr. f. d. ges. Neurol. u. Psychiat. **145**:208, 1933.

Some nerve fibers in the immediate vicinity of the tumor lose their myelin sheaths so that the axis-cylinders fall out, and some of them show fragmentation; the remote fibers remain intact. An intracranial tumor may influence in different ways the nuclei of the brain stem known as sympathetic and parasympathetic centers, as well as those of other regions and their conducting paths. These ways are the following: 1. Growth of the mass and destruction of the diencephalic nuclei or their conducting paths. This is the most important factor. 2. Compression of these formations by the growing tumor. Such compression may be caused by either a near or a distant tumor; however, the relative stability of the ganglionic elements and their resistance to the influence of the tumor at a distance allow one to assume that if the tumor is distant the peripheral changes will be relatively insignificant or will be absent. 3. Disease of the vessels supplying a certain region of the brain stem, followed by an infarction in the corresponding area. 4. Obstruction by the tumor of the paths of communication of the cerebrospinal fluid, followed by distention of the third ventricle and atrophy of its base, of the region of the tuber cinereum and of the nuclei corporum mamillarium in the region of the autonomic centers.

In describing peripheral diseases of the autonomic nervous system one must take into account the fact that clinical researches (Zakharchenko;[23] Tumskoy;[24] Blumenau[25]) indicate the presence of crossed fibers running from the diencephalic nuclei. Probably the crossing of vegetative fibers, as well as that of more highly differentiated descending systems such as the pyramidal tract, Löwenthal's tract or Monakow's tract, is not complete. Therefore, a pathologic process developing above the site of the crossing will also be more or less manifested on the side homolateral to its localization. In the spinal cord the descending autonomic systems apparently are partly or completely interrupted in Jacobson's centers of the lateral horns; they pass through the anterior roots of the rami communicantes to the sympathetic trunk, its ganglions and the prevertebral ganglions.

My pathoanatomic researches have been carried out on material obtained from 21 patients: 18 who died of tumor of the brain, 1 who died of meningitis, 1 who died of abscess of the cerebellum and 1 who died of hydrocephalus.

Tumors of the brain occurring in this series may be divided into the following types: glioma, 10; ganglioneuroma, 1; meningioma, 2; neuri-

23. Zakharchenko, M. A.: Sosudistye zabolevanja mozgovogo stvola, Moskow, G. F. Smirnov, 1911.

24. Tumskoy, V. A.; Ostapovitsch, G. D., and Semenov, S. S.: Kazan. m. j. 28:97, 1933.

25. Blumenau, L. W.: Anatomo-physiol. vvedenie v clinicu nervnich boleznei, Moskow, Gosisdat, 1925.

noma, 1; metastatic sarcoma, 1; metastases from carcinoma, 3. I have investigated both superior cervical ganglions, the stellate ganglions, the solar plexus and the trunks of the vagus nerve and its ganglion nodosum; in a number of cases vagal nuclei of the medulla and nuclei of the hypothalamic region have been studied. I have applied the method of staining the frozen sections described by Filatowa and Lawrentjew [26] after Bielschowsky and Gros. Some preparations have been after-stained with hematoxylin or sudan. In some cases I have stained the myelin by the method of Spielmeyer; the cells have been stained according to Nissl's method.

As for my microscopic observations, in 4 cases I saw on the autopsy table phenomena which may be considered dystrophic: hemorrhage in the gastric wall in 2 cases and agonol autolysis of the gastric and esophageal walls in 2 cases. In the brains of the 4 cadavers I observed the brain stem invaded by the tumor in 2 instances; in 2 instances the brain stem was under considerable pressure.

Zenker [27] and Brosch [28] have also noticed autolysis of the gastric and esophageal walls in cases of disease of the brain stem.

It is necessary to point out that dystrophic alterations at the periphery have not always been followed by changes in the sympathetic ganglions. In 2 instances I observed peripheral trophic disturbances in the form of hemorrhage in the gastric wall and agonal autolysis of the gastric wall without any considerable alteration in the solar plexus. Obviously, dystrophic changes in the digestive tract may occur without morphologically visible disease of the collectors of autonomic innervation. A deeper and more prolonged dystrophic process, such as penetrating or perforating gastric ulcer, is followed by alterations of the nervous system similar to those observed in cases of tumor of the brain. This is most obvious in the study of the solar plexus.

Among the pathologic phenomena observed in the solar plexus, the attention is drawn by the *Kugelphänomen,* the formation of peculiar thin rings and small "loops." These formations are caused by breaking down of the pericellular apparatus, destruction of the neurofibrillar cellular apparatus, pyknotic alterations of the nucleus, formation of swellings or varicosities on the fibers and vacuolation and disaggregation of the fibers. Disease of the fibers and cells in the solar plexus has been observed much less frequently than in the ganglions of the sympathetic trunk and mainly in cases of cancer.

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26. Filatowa, A. G., and Lawrentjew, B. I.: Virchows Arch. f. path. Anat. **286**:1, 1932.

27. Zenker, in von Ziemssen, H.: Handbuch der speziellen Pathologie und Therapie, Leipzig, F. C. W. Vogel, 1877, vol. 7.

28. Brosch, cited in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1926.

A considerable development of the *Kugelphänomen* in the solar plexus has been discovered in 8 cases of tumor of the brain. In the vicinity of some cells from two to five *Kugeln* may be seen. Besides those detected in the immediate proximity of the cells, some isolated *Kugeln* have been observed among the bundles of fibers. In 5 cases, together with the *Kugeln* I have detected hollow "rings;" in some they were connected with fibers and formed small "loops" (figs. 1, 2 and 3).

In these 5 cases I have observed invasion or compression of the brain stem by the tumor on the level of the anterior part of the medulla oblongata and the pons.

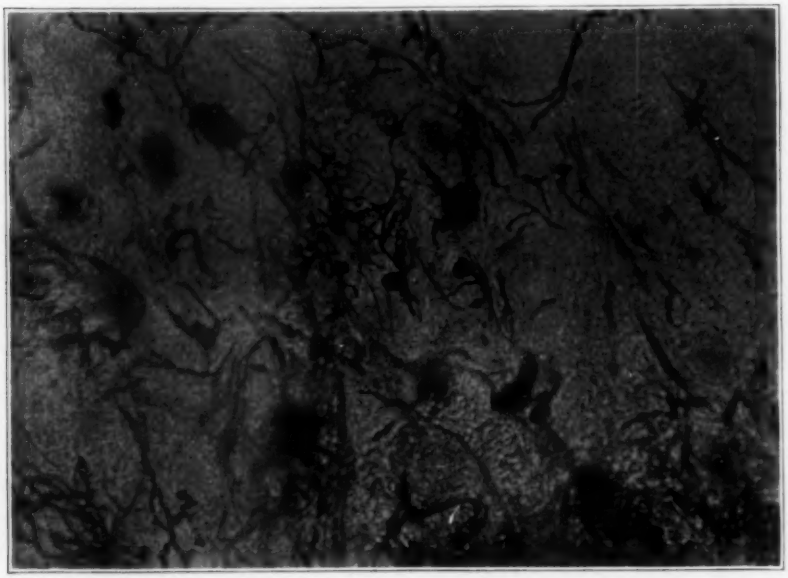

Fig. 1.—Photomicrograph of *Kugelphänomen* observed in the solar plexus of a patient with tumor of the pineal gland. Gros-Bielschowsky stain; Zeiss ocular 4 Ob. D.

In 10 cases the *Kugelphänomen* was slightly developed. In 2 of these cases compression of the medulla was observed. As some of the patients in whom a small number of *Kugeln* were detected were much older than the majority of those in whom *Kugeln* were more numerous, one cannot consider this pathologic phenomenon exclusively a sign of age involution. One may consider, as a control, preparations of the solar plexuses of patients with disease of the lungs, in which the *Kugelphänomen* has also been rarely found. For comparison, I stained the semilunar ganglions of 2 patients with cancer of the stomach, of 1 with cancer of the biliary passages and of 2 with gastric ulcer (1 of these died from shock while I was isolating an ulcer penetrating into the pancreas;

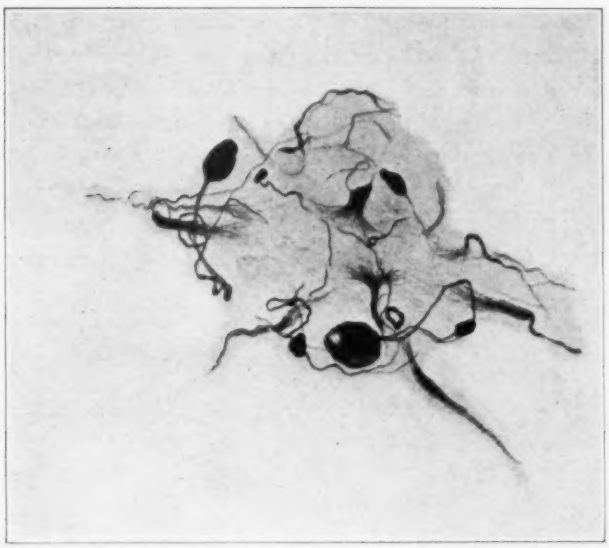

Fig. 2.—Drawing of *Kugeln* and "Rings" observed in the solar plexus of a patient with a tumor of the cerebellum. Gros-Bielschowsky stain; Zeiss homogeneous immersion.

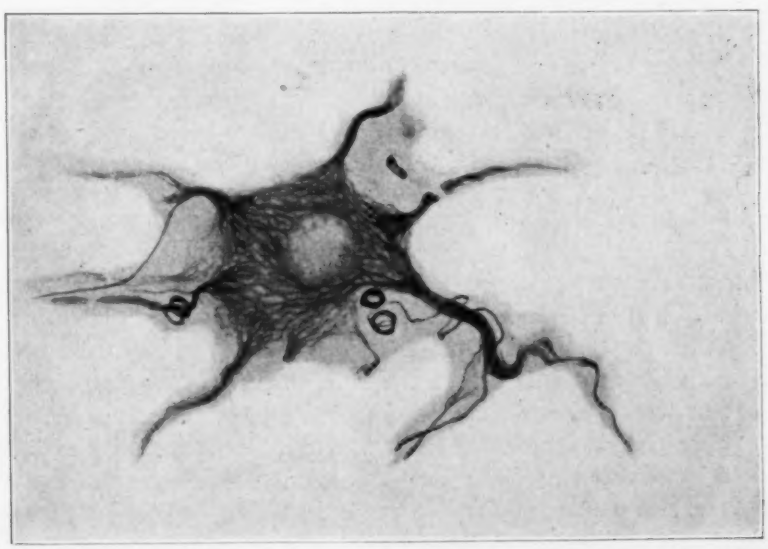

Fig. 3.—Drawing to show the breaking down of the pericellular apparatus of the right stellate ganglion in a patient with tumor of the occipital lobe. Gros-Bielschowsky stain; Zeiss homogeneous immersion.

another, with a perforating ulcer of six hours' duration, died from aspiration of the vomited matter on the first day after operation).

The most marked development of the *Kugelphänomen* was observed in cases of cancer of the biliary passages. The whole visual field was speckled with *Kugeln,* a picture which probably was connected with invasion and destruction by the tumor of a great number of postganglionic trunks passing inside the hepatoduodenal ligament. In other cases the *Kugelphänomen* was less developed but rather marked. Particular interest was afforded by the presence of a great number of "loops" and "rings" in preparations of the solar plexus of a patient with a perforating ulcer, the loops and rings having the same form but being more numerous, as in the aforementioned cases of the tumor of

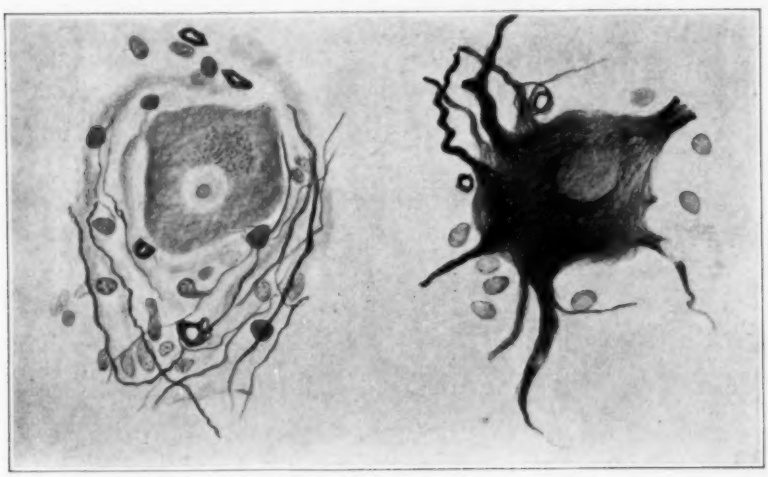

Fig. 4.—Drawing of "rings," derivatives of the synapses, in the celiac ganglion in a case of ulcus ventriculi perforans. Gros-Bielschowsky stain; Zeiss homogeneous immersion.

the brain (fig. 4). It is possible that this coincidence is the result of a kind of qualitative standardization of the morphologic reaction of the solar plexus to pathologic impulses in general, that is, impulses received from the center as well as from the periphery. It may be that confirmation of the theory (Lancereux;[29] Vulpian,[30] Burdenko) of the neurogenic central genesis of some forms of round ulcer lies in this uniformity of reaction of the solar plexus in cases of tumor of the brain and peripheral disease (gastric ulcers and cancer of the stomach).

29. Lancereux: Gaz. d. hôp. **49**:314, 1876.

30. Vulpian, E. F. A.: Léçons sur l'appareil vaso-moteur (physiologie et pathologie), Paris, Germer-Baillière, 1875, vol. 1.

It may be assumed that changes of central origin in the solar plexus at a certain stage of development, in the presence of additional irritation or without it, lead to peripheral dystrophy in the form of round ulcers. Frequently observed hyperhidrosis and pilomotor reactions, as well as symptoms of so-called vagotonia, indicate that in cases of gastric ulcer one must suspect processes of destruction in the autonomic nervous system. Apparently, the gastric ulcer may sometimes be a sign of disturbance of the peripheral trophic action as a result of disorders of the central region of the vegetative system, not always accessible to the rough methods available for morphologic investigation. In the ganglions of the sympathetic trunk the changes did not differ qualitatively from

Fig. 5.—Photomicrograph of varicose fibers of the left stellate ganglion, observed in a patient with a tumor of the cerebellopontile angle. Gros-Bielschowsky stain; Zeiss ocular 7 Ob. D.

those in the solar plexus. Pathologic changes were observed (particularly in cases of primary tumors of the brain) in fibers and in stellate ganglions, which are the most important collectors of autonomic innervation. Alterations of the fibers were found at different stages of development, from the appearance of varicosities and the formation of vacuoles to complete disintegration. The affected fibers exhibited a group arrangement; they also formed bundles (figs. 5 and 6). In cases of tumor of cortical or subcortical localization in the temporoparietal or occipital region (3 cases) the fibers were symmetrically affected on the side of occurrence of the tumor as well as in the ganglion of the opposite side. Peripheral alterations of the fibers in the ganglions obvi-

ously occur as a result of disease of the autonomic nerve paths emerging from the affected zone. One may assume that not all these paths are crossed. Thus, the pathologic impulse from the cortex is transmitted more or less uniformly to both stellate ganglions. The predominance of crossing phenomena and the occurrence of alterations in the fibers in 1 case of tumor, in which the growth destroyed the internal capsule and exerted pressure mostly on the hypothalamic region of one side, confirm the presence of crossing of the vegetative paths in the brain stem below the hypothalamic region. This case leads me to suppose that the majority of the fibers of the affected central vegetative pathway

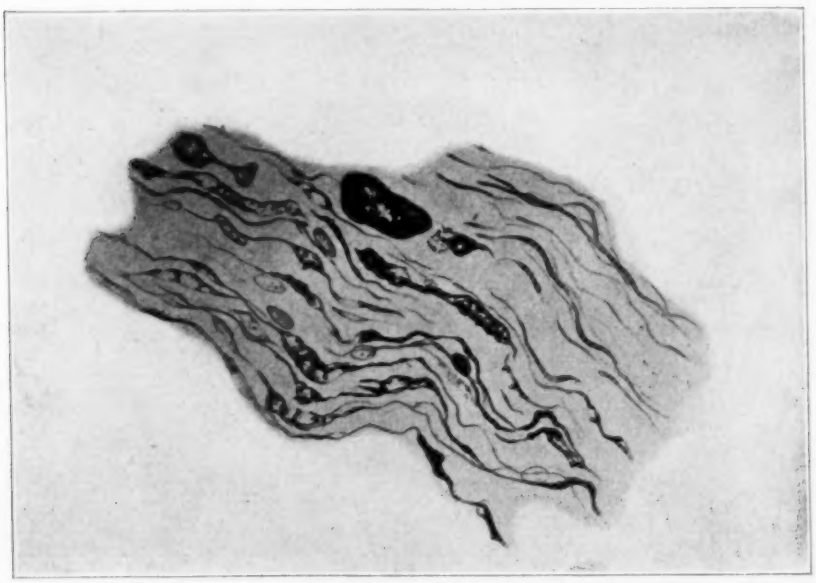

Fig. 6.—Photomicrograph showing the disaggregation of fibers in a patient with a tumor of the cerebellopontile angle; Zeiss ocular 7 Ob. D.

arising in the hypothalamic region take part in crossing. The prevailing homolateral character of the alterations in the fibers of the stellate ganglions when the central disease is localized in the pons and the more caudal regions of the brain stem (2 cases) confirms the statement that crossing in the autonomic conducting paths takes place mainly somewhere caudad to the hypothalamic region, so that a considerable number of these fibers run in the region of the pons after having been crossed. Disease of the system below the crossing produces peripheral radiation on the same side.

Probably only a small number of the fibers of the autonomic pathway cross below, in the medulla, which may be the cause of alterations in the fibers (although found in a much smaller number) also in the

contralateral stellate ganglion in cases of localization of the tumor at the level of the pons. The influence of the tumor on the vermis in 2 cases was followed by symmetric alterations in the fibers of the autonomic nervous system. The disease is probably associated with disease of some central neurons of the autonomic system. The localization of the cell bodies of these neurons is imputed to the cerebellum by a number of authors (Mikhilson and Tihalskaja).[31]

In cases of frontal tumor, of which there were 3, and in 1 case of supracerebellar subtentorial tumor, because of the relatively great distance of the tumor from the autonomic centers of the diencephalon and the brain stem and their pathways and because of the resistance of the latter to the action of the distant tumor, I did not observe any alterations in the preganglionic systems of the fibers in the sympathetic ganglions.

In the fibers and in the nuclei of the vagus nerve in cases of unilateral localization of the disease of the diencephalon and the pons, the alterations were manifested for the most part contralaterally (3 cases). This probably occurred as a result of crossing of the thalamonuclear pathways descending to the nuclei of the vagus nerve in the medulla at a relatively low level, above the zone of localization of these nuclei. Thus, in my cases the central paths had been affected before the fibers passed to the other side. The pathologic stimulus provoking irritation and degeneration apparently passes through the synapses to the cells of the nuclei dorsales et ambiguui of the vagus nerve and then to the axons of these cells.

In these 2 cases I observed peculiar pyknomorphous alterations in the cells of the dorsomedial nuclei of the vagus nerve on the side opposite the tumor; they diminished in size and lengthened (figs. 7 and 8). The alterations detected in the fibers of the sympathetic ganglions and the trunk of the vagus nerve are not at all qualitatively specific for cases of brain tumors. There is only one particularity to be noticed, namely, the aforementioned relative quantitative lateralization of the process (its unilateral development).

In my material, in the presence of a primary tumor of the brain arising from its supporting tissues, elements of generalized intoxication resulting from disintegration of the tumor, such as are observed in general infections in cases of cancer, were almost absent. In no case have I observed acute or chronic processes in the internal organs which might be considered factors in the development of alterations in the sympathetic fibers. My own material, obtained from investigation of the sympathetic ganglions in cases of pulmonary abscess and suppurative

31. Mikhilson, A. I., and Tihalskaja, W.: Russk. phy. j. **16**:466, 1933.

bronchiectasis, shows few alterations and allows me to establish relative persistence of the sympathetic fibers.

I cannot state that there is any relation of the alterations observed in the peripheral autonomic system in my material to surgical intervention. There was an exception in 1 case, in which after dissection of the vermis considerable alterations were observed in the fibers.

For a more detailed study of the influence of surgical trauma I have performed a trephination of the skull in the temporoparietal region in 7 dogs. Mixed anesthesia was used, ether, chloroform and alcohol being employed. After section of the dura mater, glass sticks were introduced under the tuber cinereum in 4 dogs and under the temporal

Fig. 7.—Photomicrograph of the base of the fourth ventricle. Note the invasion of the left half of the brain stem by the tumor at the level of the pons. Nissl stain; Zeiss ocular 7 Ob. A.

lobe near the tuber cinereum in 3 dogs. Three animals died three days after operation (1 from meningitis), and 4 animals were killed after periods varying from nine to fifteen days. In 2 dogs I discovered an insignificant number of varicose fibers in the trunks of the vagus nerve. In all the dogs the fibers of the sympathetic ganglions were observed to be normal, although 1 of the animals had a round duodenal ulcer and 2 had a hemorrhage in the mucous membrane of the small intestine. The last circumstance makes me emphasize the relative resistance of the fibers of the sympathetic ganglions to the pathologic influence. As regards the hydrocephalus, I attribute only an insignificant role to that

factor because of the aforementioned resistance. This is confirmed by the fact that in 3 cases in which considerable hydrocephalic changes were observed there was almost no reaction of the preganglionic systems of the fibers. Thus, the probable cause of the alterations detected in the fibers in my cases was disturbance of the central neurons of the autonomic nervous system by the tumor, which resulted in involvement of the concomitant peripheral neurons.

I have discovered in 2 patients a considerable number of *Kugeln* in the ganglion nodosum of the vagus nerve on the side of localization of the process in the brain; in the vicinity of some cells five or six *Kugeln* have been found.

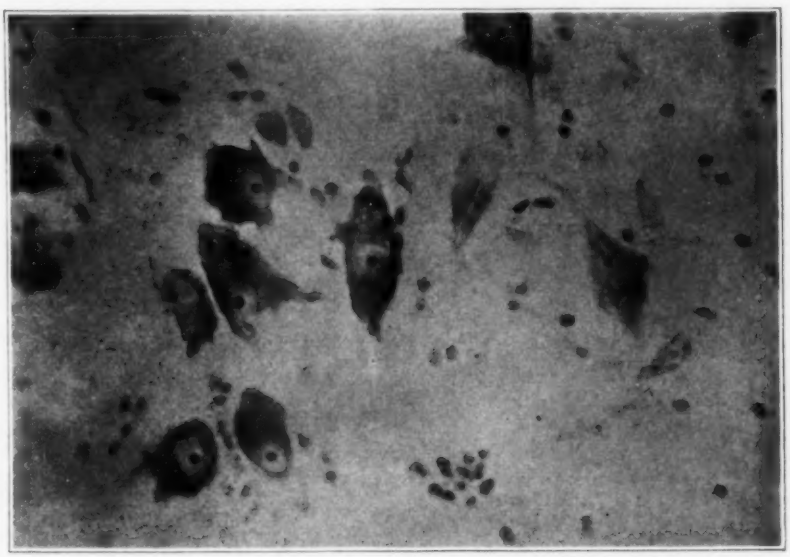

Fig. 8.—Photomicrograph of the nucleus dorsomedialis of the left vagus nerve (side of localization of the tumor). Nissl stain; Zeiss ocular 7 Ob. D.

In the first case one must suppose that because of a stronger compression of the root of the vagus nerve on the side of occurrence of the abscess, the axons of the cells of the corresponding ganglion nodosum were affected and a homolateral *Kugelphänomen* was considerably developed. Homolateral development of the *Kugelphänomen* in the ganglion nodosum was observed in 1 patient with bronchiectasis mainly on the side on which the lung was affected. Several hours before death an injection of procaine hydrochloride was made into the trunk of the vagus nerve, and a lobectomy was performed.

In cases of cancerous metastases, in which degenerative phenomena have been most frequently observed, an accumulation of satellites occasionally was detected around the degenerated cells.

As regards malignant tumor, it must be emphasized that alterations in the fibers and cells may be caused in a great measure by generalized toxic or reflex influences associated with the disintegration and, in fact, with the very existence of the cancerous neoformation, as has been observed by Borowsky.[32] In 3 cases I observed an increased deposit of argentophilic pigment in the nerve cells of the sympathetic ganglions in persons from 12 to 24 years of age.

Herzog,[33] De Castro[34] and Chodos[35] stated that the increased accumulation of pigment is associated with diseases causing generalized exhaustion. Symptoms of such exhaustion, which pathogenetically may somewhat resemble cerebral cachexia, were also observed in my patients.

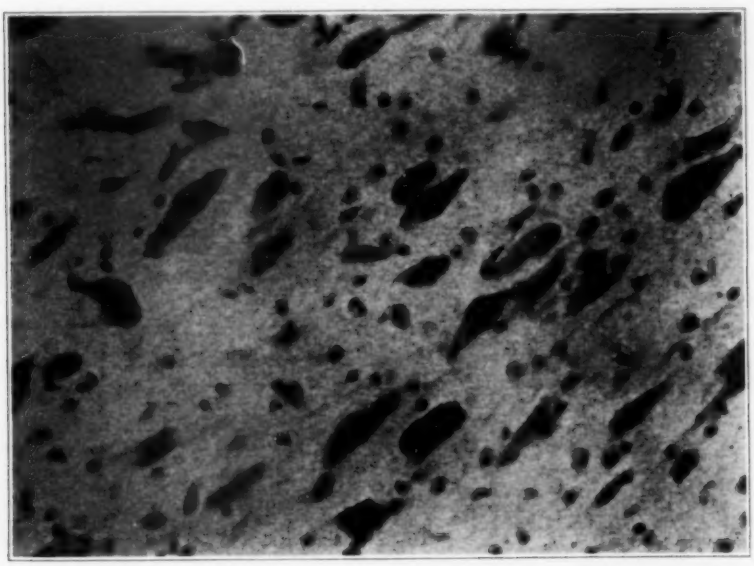

Fig. 9.—Photomicrograph of the nucelus dorsomedialis of the right vagus nerve (contralateral to the tumor). Nissl stain; Zeiss ocular 7 Ob. D.

Nevertheless, in other cases, in which little pigment was found in the cells of patients with generalized exhaustion, I had apparently to deal with an individual instability of metabolism in the nerve cells.

In 4 patients with tumors of the brain I have discovered single vacuoles and coarseness of the fibrillar structure in the cells. Very rarely (one in a preparation or in several preparations) I have observed

32. Borowsky, M. L.: Ztschr. f. d. ges. Neurol. u. Psychiat. **146**:692, 1933.
33. Herzog, E.: Ztschr. f. d. ges. Neurol. u. Psychiat. **103**:1, 1926.
34. De Castro, F.: Sympathetic Ganglia, Normal and Pathological, Madrid, 1927.
35. Chodos, C. G.: Ztschr. f. d. ges. Neurol. u. Psychiat. **135**:358, 1931.

cells entirely filled with vacuoles, changed and degenerated. Some of the diminished cells had pyknotic nuclei and pale protoplasm.

In 6 cases of intracranial tumors with rather strongly manifested irritation and degeneration of the preganglionic fibers in the stellate ganglions I have detected phenomena of perinuclear tigrolysis, as well as of complete tigrolysis with group arrangement of the altered cells. In a lesser degree these phenomena in the ganglionic cells have been noticed by me in other patients with cerebral disease.

In the aforementioned experiments I observed in all cases a well marked perinuclear tigrolysis and sometimes complete tigrolysis. No lateralization of the process similar to that observed in disease of the fibers could be found in the arrangement of cells with tigrolysis. This circumstance, together with the lability of the tigroid substance in the nerve cells and a pheochrome type of granulation, leads me to attribute the phenomenon of tigrolysis to the general influence of the tumors on the vegetative centers, the surgical intervention, hunger and possibly other factors which may have escaped my attention.

SUMMARY

1. Phenomena of degeneration and irritation in the neural elements of the solar plexus are found mostly in cases of disease of the brain stem and are not always followed by dystrophic alteration of the tissues.

2. The qualitative features of the pathologic changes observed in the sympathetic and parasympathetic systems in the presence of tumor of the brain do not differ from those observed in the same regions of the nervous system in cases of disease of the peripheral organs.

3. In case of localization of the tumor in the region of the pons the changes in the fibers of the sympathetic ganglions are revealed mostly in the ganglions on the side of localization of the intracranial tumor.

4. In case of cortical localization of the tumor of the temporoparietal region, as a result of a partial crossing of cortical descending systems the changes exhibit symmetry.

5. In 1 case of hypothalamic tumor, neoformed alterations of the fibers prevailed in the stellate ganglion of the side opposite the tumor.

6. The alterations in the cells of the autonomic system exhibited a focal character and maintained a certain symmetry in the qualitative development of the process.

7. As a result of a low localization of the crossing of cortical and thalamonuclear pathways in cases in which neoformations were localized in the brain stem the fibers of the vagus nerve were for the most part affected contralaterally.

FRACTURES OF THE PELVIS

ANALYSIS OF SEVENTY-NINE CASES

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This is a review of cases in which fracture of the pelvis was treated at the Harlem Hospital from Dec. 1, 1933 to Dec. 1, 1937. It is a continuation of a study made by Conway.[1]

CAUSE OF INJURY

Seventy-nine patients with fracture of the pelvis, were admitted to the hospital within the period mentioned. Of these, 55 were males and 24 females, the ages ranging from 3 to 83 years. The age incidence is given in table 1.

It will be noted that the greatest number of patients entered the hospital when they were within the decade from 20 to 30 years. This decade is the most active period of life, when the patient is most susceptible to trauma.

The causative traumas are listed in table 2.

In this series, 39 patients were admitted to the hospital after having fallen or jumped from a height, such as a roof, fire escape, a window (first to fifth story), a flight of stairs or an elevator shaft. The second most important factor in causation of fractures of the pelvis is the automobile. Twenty-eight of the patients had been struck by an automobile. In 4 cases the cause of fracture was unknown; in these the patient's condition was so serious that he was unconscious when admitted, or was under the influence of alcohol. In 1 case the fracture was caused by a gunshot wound in which there were multiple perforations of the left ilium, the bladder also being punctured. The patient in this case died four days later from peritonitis even though a laparotomy was done to close the vesical openings. Four patients had crushing injuries. One was caught between two "L" cars and had other multiple

From the Surgical Service of the Harlem Hospital, Dr. Louis T. Wright, Director.

1. Conway, F. M.: Fractures of the Pelvis: Clinical Study of Fifty-Six Cases. Am. J. Surg. **30**:69 (Oct.) 1935.

fractures. One patient was injured by the overturning of an automobile in which he was riding. One patient was struck with a steam bucket weighing 3 tons while he was handling coal. One patient had been assaulted.

ASSOCIATED INJURIES

In many cases of fracture of the pelvis the patient is unconscious, and roentgenograms of the entire osseous system are necessary. Complications, such as intracranial injuries and internal thoracic and abdomi-

TABLE 1.—*Age Incidence in Seventy-Nine Cases of Fracture of the Pelvis*

Age, Years	Number of Patients
1 to 10	6
10 to 20	13
20 to 30	30
30 to 40	12
40 to 50	10
50 to 60	4
60 to 70	2
70 to 80	1
80 to 90	1

TABLE 2.—*Causes of Fracture in This Series of Cases*

Cause	Number of Cases
Patient jumped or fell from a height	39
Patient struck by auto (taxicab, private car, motorcycle, truck)	28
Cause unknown	4
Patient shot	1
Patient caught between "L" cars	1
Patient fell from truck; run over by wheels	1
Patient injured in overturning automobile	1
Patient run over by wagon	1
Patient struck by coal bucket (3 tons)	1
Patient assaulted	1
Patient struck by subway train	1
Total	79

nal injuries, must be considered. Patients admitted to the hospital in a state of shock must be treated for shock even before treatment is given for fracture of the pelvis or associated fractures.

ANATOMIC CLASSIFICATION

In the anatomic classification of the fractures in this series of cases the terminology of Noland and Conwell has been followed (table 3).

PERIOD OF HOSPITALIZATION

Twenty-six of the 79 patients had fractures of the pelvis only; that is, there were no associated injuries. Of these 26, 2 had diabetes. We

are sure that this condition prolonged their stay in the hospital. However, including these 2 patients, for whom the period of hospitalization was fifty-two and eighty-four days respectively, the average period of hospitalization was twenty-six days. If these 2 patients are eliminated the average period of hospitalization for each of the remaining 24 patients was twenty and eight-tenths days (table 4). On the other hand, the average period of hospitalization for patients with fracture of the pelvis with associated injuries was forty-eight and three-tenths days. In other words, it was usually the associated injury and not the pelvic fracture which caused the prolonged hospitalization.

DIAGNOSIS

There is a definite method of examination to determine whether a fracture of the pelvis is present. With the patient in the recumbent

TABLE 3.—*Anatomic Classification of Fractures*

Injury	Left	Right	
Fracture of ala of ilium	7	7	
Fracture of crest of ilium	3	4	
Fracture of superior ramus of pubic bone	25	24	
Fracture of inferior ramus of pubic bone	21	13	
Fracture of inferior ramus of ischium	5	2	
Fracture of superior ramus of ischium	2	1	
Fracture of acetabulum	6	6	
Definite sacroiliac separation	4	4	
Separation of symphysis pubis			8
Isolated fracture of the ischial tuberosity			0
Double vertical fracture of the pelvis (Malgaigne)			3
Fracture of the sacrum with associated pelvic fracture			7

position, one presses down on the anterior superior spines, or, by alternating this pressure, one rocks the pelvis. Pressure medially on the crests of the iliums or pressure directly downward over the symphysis pubis may, by eliciting pain, give a fairly definite indication as to whether or not a fracture exists. For fracture in the region of the acetabulum, by elevating, lowering, abducting, adducting, externally rotating and internally rotating the lower extremity one may obtain a fair idea of any existing pathologic condition. However, the final diagnosis depends on roentgen study, which certainly is a safer procedure.

DIAGNOSIS OF ASSOCIATED VISCERAL INJURY

When a patient has fallen from a third or fourth story window or who has been struck by an automobile, bloody urine is indicative of a pathologic condition which may exist anywhere along the genitourinary tract, from the kidney to the glans penis. Frank blood is passed in the presence of rupture of the urethra. If an attempt is made to pass a

TABLE 4.—*Uncomplicated Fracture of the Pelvis*

Patient	Age	Sex	How Injured	Type of Pelvic Injury	Days in Hospital	Result
M. G.	22	M	Struck by truck	Fracture of ascending ramus of left pubic bone at junction with ischium; fracture of sacrum near sacroiliac articulation	22	Improved
N. M.	7	M	Struck by automobile	Fracture of ascending ramus of right pubic bone at junction and ischium; relaxation of right sacroiliac joint	18	Improved
M. A.	20	M	Fell from roof	Transverse fracture of midportion of right ilium	1	Unimproved; transferred
P. B.	23	M	Automobile overturned with patient	Fracture of right side of symphysis pubis	7 AOR*	Improved
J. J.	25	M	Fell ten stories	Fracture of right ilium	3	Died p.m.; hypostatic pneumonia
J. D.	72	M	Struck by truck	Fracture of right ilium, right acetabulum and right superior ramus of pubis	45	Improved
J. Mc.	23	M	Fell from truck; wheels ran over him	Fracture of left ischium and left pubis near symphysis	9 AOR	Improved
A. G.	48	F	Fell on street	Fracture of left ischium	7 AOR	Improved
M. F.	35	F	Fell 1 story	Fracture of both rami of right pubic bone; fracture of crest of right ilium into sacroiliac joint	12 AOR	Improved
D. P.	61	F	Fell in kitchen	Fracture of ascending ramus of right pubic bone	20	Improved
V. S.	27	F	Struck by automobile	Fracture of descending ramus of left pubic bone	35	Improved
E. C.	4	F	Struck by taxicab	Oblique fracture of left pubic bone	30	Improved
E. T.	26	F	Fell 2 stories	Oblique fracture of junction of inferior rami of right ischium and pubic bone; fracture of left ilium near upper part of left sacroiliac joint	50	Improved
M. G.	24	F	Jumped from car	Fracture of ascending ramus of right pubic bone	17	Improved
G. C.	11	M	Struck by automobile	Fracture of body of right and left pubic bones and descending ramus of left pubic bone	12	Improved
G. L.	44	F	Struck by automobile	Fracture of left pubic bone; free bone in region of fracture; fracture of right ischium; patient diabetic	52	Improved
A. R.	59	F	Struck by automobile	Fracture of superior rami of both pubic bones and left ilium near sacroiliac joint; patient diabetic	84	Improved
G. Y.	13	F	Fell 1 story (elevator shaft)	Diastatic fracture of right ilium from crest to tip of sacroiliac articulation; widening of symphysis	35	Improved
R. D.	5	M	Struck by truck	Fracture of descending ramus of right pubic bone	57	Improved
E. W.	50	M	Struck by car	Fracture of left acetabulum	35	Improved
P. R.	30	F	Fell 2 stories	Fracture of ascending and descending rami of left pubic bone	27	Improved
O. C.	14	M	Struck by truck	Fracture of superior ramus right pubic bone	16	Improved
E. V.	14	F	Fell 1 story	Fracture of left pubic bone	5	Improved
H. I.	46	M	Struck by car	Fracture of right pubic bone	41	Improved
J. J.	41	M	Fell 1 story	Fracture of right pubic bone near symphysis	15	Improved
H. R.	29	M	Struck by taxicab	Fracture of midportion of body of sacrum and of right ilium	40	Improved
R. D.	26	M	Fell from car	Fracture of inferior ramus of left pubic bone	17	Improved

* In this table and in the following tables, the abbreviation AOR denotes "at own risk."

TABLE 5.—*Analysis of Cystograms*

Patient	Age	Sex	Cause of Injury	Type of Pelvic Fracture	Cystogram	Urine	Results
1.	23	F	Fell from 3d story	Fracture of right ilium, ascending and descending rami of both pubic bones	Displacement of bladder to left; no evidence of extravasation	Occasional red blood cell	Improved
2.	24	M	Struck by automobile	Fracture of superior ramus of left pubic bone; separation of symphysis pubis	No evidence of vesical injury	No red blood cells	Improved
3. J. H.	11	M	Wagon ran over abdomen	Separation of symphysis pubis	No vesical injury	No red blood cells	Improved
4.	38	M	Fell from fire escape, 4 stories	Multiple fractures of right ilium, extending into sacroiliac joint; fracture of ascending and descending rami of right pubic bone	No vesical injury; incomplete filling of pelvis and calices of right kidney; dilatation of right ureter	Bloody	Improved
5.	30	M	Fell down stairs	Fracture of descending ramus of left pubic bone	Bladder filled normally	No red blood cells	Improved
6.	40	M	Struck by motorcycle	Fracture of body, ascending rami and descending rami of left ischium; fracture of left acetabulum	No vesical injury	Few red blood cells	Improved
7. E. S.	62	M	Fell from wall	Fracture of ascending and descending rami of left pubic bone	Bladder filled normally	No red blood cells	Improved
8.	25	F	Unknown	Fracture of ascending and descending rami of left pubic bone; fracture of right acetabulum; separation of right sacroiliac articulation	Bladder normal	No red blood cells	Improved
9.	23	M	Fell from a truck; wheels ran over him	Fracture of left ischium and left pubic bone near symphysis	Bladder normal	Bloody	Improved
10.	35	M	Fell 1 story	Fracture of both rami of right pubic bone and crest of right ilium into sacroiliac joint	Bladder filled normally	No red blood cells	Improved
11.	13	F	Fell down elevator shaft, 1 story	Diastatic fracture of right ilium from crest to sacroiliac articulation	Bladder filled normally	No red blood cells	Improved
12.	30	F	Fell 2 stories	Fracture of ascending and descending rami of left pubic bone	Compression on left side and hemorrhage	Bloody	Improved
13.	26	M	Fell from car	Fracture of inferior ramus of left pubic bone	No abnormality	Clear	Improved
14.	46	M	Struck by car	Fracture of right pubic bone	No abnormality	Clear	Improved
15.	41	M	Fell 1 story	Fracture of right pubic bone near symphysis	No abnormality	Clear	Improved
16. S. W.	14	M	Run over by truck	Separation of symphysis pubis; separation of right sacroiliac joint; fracture of superior ramus of right pubic bone	Unsuccessful	Frankly bloody	Improved

TABLE 6.—*Vesical and Urethral Injuries*

Patient	Age	Sex	Cause of Pelvic Fracture	Type of Pelvic Fracture	Associated Injuries	Vesical Injuries	Urethral Injuries	Treatment	Time in Hospital	Result
E. B.	23	M	Gunshot	Perforating fracture	Perforation of					

TABLE 6.—*Vesical and Urethral Injuries*

Patient	Age	Sex	Cause of Pelvic Fracture	Type of Pelvic Fracture	Associated Injuries	Vesical Injuries	Urethral Injuries	Treatment	Time in Hospital	Result
E. B.	23	M	Gunshot	Perforating fracture of left ilium	Perforation of bladder	Yes	No	Laparotomy	4 days	Died of peritonitis
P. B.	33	M	Automobile overturned	Fracture of right pubic bone (superior ramus)	None	None	Yes	Rest in bed	7 days (AOR)	Improved
A. T.	27	M	Struck by automobile	Comminuted fracture of wing of left ilium	Fracture of 11th and 12th ribs posteriorly; fracture of left 8th rib, posterior axillary line; fracture of left ulna	? Urine bloody	?	Rest in bed	3 days	Transferred to Bellevue; traumatic delirium
F. D.	30	M	Fell 5 stories	Fracture of ascending ramus of left pubic bone; fracture and dislocation of left sacroiliac articulation	Spiral comminuted fracture of upper half of shaft of left femur; fracture of transverse processes of 1st and 5th lumbar vertebrae	? Had bloody urine on admission; was observed for distention and extravasation; condition cleared up	?	Double Russell traction	50 days	Improved
C. J.	48	F	Struck by taxicab	Fracture of ascending ramus of right pubic bone	Fracture of left femur	Yes	No	Repair of ruptured bladder; Russell traction	Still confined (60 days)	Good
W. B.	24	M	Struck by automobile	Fracture of right and left pubic bones; extending into left acetabulum	Abrasions of face, arms and chin; lacerations and contusions of right side of head; subarachnoid hemorrhage; retroperitoneal hemorrhage; rupture of bladder and membranous portion of urethra with laceration of prostate and anterior wall of rectum	Rupture of bladder and urethra		Treatment for shock	11 hr.	Died
S. W.	14	M	Run over by truck	Separation of symphysis pubis; separation of right sacroiliac joint; fracture of right superior ramus of pubis	Rupture of urethra; complete fracture of 4th and 5th lumbar vertebrae	Rupture of bladder and urethra		Conwell sling; suprapubic urethroplasty	3 mo.	Improved
A. B.	27	F	Fell 3 flights	Fracture of pubis on both sides; fracture of acetabulum	Fracture of lower end of right humerus and anterior lip of ulna; rupture of spleen; rupture of fundus of urinary bladder	Rupture of bladder	No	Laparotomy	6 hr.	Died

catheter in a completely severed uretha an obstruction will be observed to prevent the catheter from passing. If the rupture is partial there may be some difficulty in passing the catheter, but usually, after some difficulty, it can be made to pass.

The bladder may rupture intraperitoneally or extraperitoneally. Extraperitoneal rupture is usually in the space of Retzius. In this case extravasation may extend upward over the lower anterior portion of the abdominal wall as high as the umbilicus or the back and down behind the rectum. Evidence of irritation and inflammation accompanies the extravasation. Intraperitoneal rupture gives evidence of peritoneal irritation, such as pain, fever and abdominal rigidity. If the

Fig. 1.—Cystogram showing normal conditions.

intra-abdominal extravasation is extensive, a fluid wave is present. An abdominal tap in most instances will confirm the diagnosis. The most important method of diagnosing rupture of the bladder is the taking of a cystogram. Two hundred and fifty cubic centimeters of a 20 per cent solution of hippuran is injected transurethrally through a catheter into the bladder. Immediately thereafter a roentgenogram is taken. If there is a rupture of the bladder the extravasated opaque material will be seen roentgenologically. If the bladder is not ruptured its normal contour will be seen. Intravenous urographic study may be considered by those fearful of introducing infection from without. In eight cases (10.1 per cent) of our series the condition was complicated by vesical or urethral injuries or both.

TABLE 7.—*Pelvic Fracture with Serious Associated Injuries*

Patient	Age	Sex	How Injured	Type of Pelvic Injury	Associated Injuries	Time in Hospital	Results
D. R.	18	F	Fell 2 flights from window	Fracture of ascending and descending rami of left pubic bone; incomplete fracture of left	Fracture of bodies of 2d and 3d lumbar verte-	60 days	Improved

TABLE 7.—*Pelvic Fracture with Serious Associated Injuries*

Patient	Age	Sex	How Injured	Type of Pelvic Injury	Associated Injuries	Time in Hospital	Results
D. R.	18	F	Fell 2 flights from window	Fracture of ascending and descending rami of left pubic bone; incomplete fracture of left ilium, above acetabulum	Fracture of bodies of 2d and 3d lumbar vertebrae	60 days	Improved
E. L.	18	M	Struck by truck	Fracture of descending ramus of right pubic bone; fracture into left acetabulum and vertical fracture through sacrum	Fracture of middle third of left clavicle; fracture of right femur, middle of shaft	66 days	Improved; exploratory laparotomy done
F. D.	30	M	Fell 5 stories	Fracture of descending ramus of left pubic bone; dislocation of left sacroiliac articulation	Spiral comminuted fracture of upper half of shaft of left femur; fracture of transverse processes of 1st and 5th lumbar vertebrae	50 days	Improved
S. A.	25	M	Fell from wagon	Fracture of superior ramus of left pubic bone	Fracture of left 7th, 8th, 9th and 10th ribs in posterior axillary line	10 days	Improved
A. C.	54	M	Fell 10 feet	Fracture of external articulating surface of sacrum at right sacroiliac joint; fracture of left acetabulum	Fracture of right transverse process of 5th lumbar vertebra	20 days	Improved
E. W.	3	F	Struck by auto	Fracture of right pubis	Laceration of perineum	37 days	Improved
J. P.	23	F	Fell from 3d story window	Fracture of right ilium, ascending and descending rami of both pubic bones	Fracture of medial intercondyloid spine of right tibia; fracture of 7th, 8th, 9th and 11th ribs on right in axillary line	34 days	Improved
W. P.	24	M	Struck by auto	Fracture of superior ramus of left pubic bone; separation of symphysis	Laceration of right thigh; chip fracture of greater trochanter of left femur	29 days	Improved
M. H.	38	M	Fell 4 stories from fire escape	Fracture of both rami of left pubic bone	Mild intracranial injury and fracture of left radius and ulna	43 days	Improved
A. L.	26	F	Struck by auto	Double fracture of right pubic bone	Multiple fractures of upper right ribs posteriorly	39 days	Improved
J. O.	34	M	Fell from 3d story window	Fracture of left ilium, acetabulum and ascending and descending rami of pubic bone	Fracture of right tibia and fibula, fracture of os calcis and of transverse process of 5th lumbar vertebra	150 days	Improved
I. B.	25	F	Unknown	Fracture of ascending and descending rami of left pubic bone; fracture of right acetabulum; separation of right sacroiliac articulation	Extensive comminuted fracture of lower third of right femur	199 days	Improved
A. A.	46	F	Fell from 3d story window	Fracture of superior rami of both pubic bones	Intracranial injury; fracture of 10th rib on left	19 days	Improved
C. T.	10	M	Fell from 3d story window	Chip fracture of superior ramus of right pubic bone	Intracranial injury; epiphysial separation of left radius	19 days	Improved
H. W.	35	M	Fell from window	Transverse fracture of ascending ramus of left pubic bone	Fracture of left radius and ulna	19 days	Improved
J. B.	15	M	Fell from 2d story window	Fracture of descending ramus of left pubic bone; also of body of left pubic bone; relaxation of left sacroiliac articulation	Fracture of left os calcis, left radius and ulna and left transverse process of 5th lumbar vertebra	47 days	Improved
C. J.	48	F	Struck by taxicab	Fracture of ascending ramus of right pubic bone	Fracture of left femur	60 days	Good
R. A.	33	M	Struck by train	Fracture of crest of left ilium	Traumatic amputation of right leg	137 days	Improved
J. G.	29	M	Fell 3 stories	Fracture of right pubic bone	Pneumothorax; fracture of right internal malleolus; fracture of right rib	35 days	Improved
T. H.	42	M	Fell 12 feet	Fracture of both pubic bones near symphysis	Fracture of left thumb	24 days	Improved
S. W.	14	M	Run over by truck	Separation of symphysis pubis; separation of right sacroiliac joint; fracture of right superior ramus of pubis	Rupture of urethra; compound fracture of 4th and 5th lumbar vertebrae	.....	Improved

INVOLVEMENT OF NERVES

A neglected factor in the study of fracture of the pelvis is the question of neural involvement. Although most patients complain of neuralgia, this symptom is only too readily ascribed to the fracture, and no thought is given to possible neural injury. Investigation, however, will frequently reveal neural trauma.

Incidence.—Not much space in the literature is given to discussion of neural injury associated with pelvic fracture. The report of one series gives the incidence as 2 per cent; other figures are as low as 0.75

Fig. 2.—Pelvic fracture which was perfectly reduced by treatment with the Conwell sling.

per cent. The incidence of neural involvement in one series, in which neural injuries were particularly watched for, was 9 per cent.

Site of Fracture.—Neural injuries occur most frequently with fractures of the posterior rim of the pelvis. One must not forget that a sacroiliac joint may have been luxated at the time of the injury and yet not show such an injury on the roentgenogram, as it may have sprung back in place so that the roentgenogram shows only the anterior ring affected.

Nerves Involved.—Nerves frequently affected are: (1) the lumbosacral cord at the pelvic brim, (2) the sciatic nerve, especially the pero-

neal component, and (3) the obturator nerve (in fracture of the anterior ring). The sciatic nerve arises from the main band of the sacral plexus. It splits in the thigh into the common peroneal and the tibial nerve. The sacral plexus is composed of the lumbosacral trunk, the anterior division of the first sacral nerve and portions of the anterior

Fig. 3.—*A*, acetabular fracture of patient E. W. (table 4). *B*, same fracture after treatment with Russell traction.

divisions of the second and the third sacral nerve. The lumbosacral trunk is composed of the anterior division of the fifth lumbar nerve and a part of the anterior division of the fourth lumbar nerve. The femoral nerve is composed of dorsal divisions of the second, the third and the fourth lumbar nerve.

Symptoms.—Neural injury causes disturbance of reflexes, motor function and sensation. Neuralgia is a common result. Disturbances of sensation are not uncommon, especially when the lateral cutaneous femoral nerve is involved. This nerve supplies the upper lateral aspects of the thigh and arises from the dorsal divisions of the second and the third lumbar nerve.

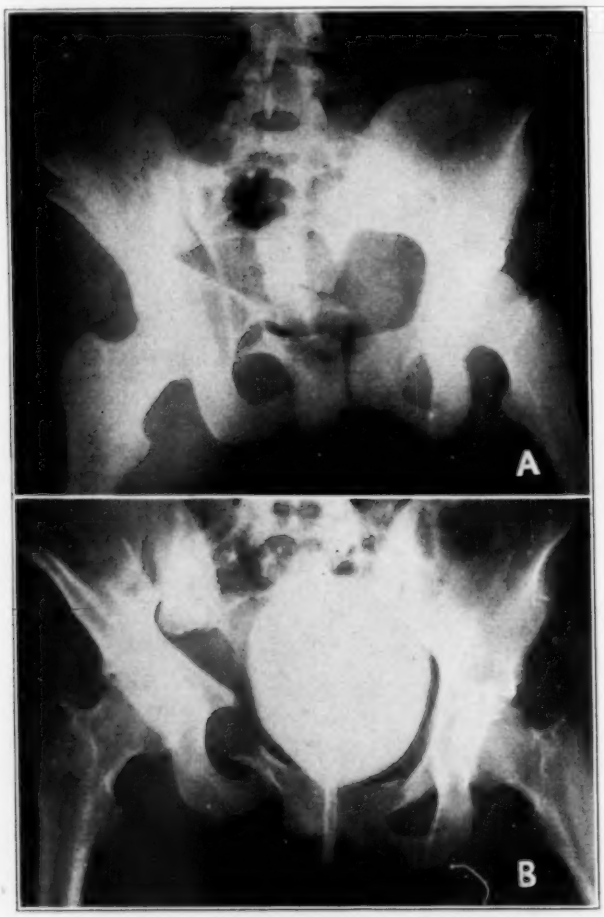

Fig. 4.—*A*, roentgenogram showing the pelvic fracture of patient (table 5). *B*, cystogram of the same patient.

When the lumbosacral plexus is involved the common symptoms are weakness of flexion of the toes, weakness of the muscles of the calf and weakness of the anterior tibial muscle. Involvement of the sacral plexus causes weakness of the muscles of the thigh, neuralgia and muscle atrophy. Involvement of the peroneal nerve gives the symptom of foot drop. Application of hot water bottles often causes burns in an anesthetic area.

Treatment.—The condition is treated with dry heat, diathermy, braces or a splint (for foot drop), and a cradle to relieve pressure from bed clothes.

End Results.—Spontaneous regeneration frequently occurs. Neuralgia and muscular weakness are the two outstanding sequelae.

Conclusion.—In every case of fracture of the pelvis careful neurologic examination is indicated to insure early institution of proper treatment.

TREATMENT OF PELVIC FRACTURE

In the main, our treatment for pelvic fracture has been simple. The uncomplicated fracture requires little more than strapping or rest in

Fig. 5.—Roentgenogram of the pelvic fracture of patient 4 (table 5).

bed. Several of our patients with separation of either the symphysis pubis or the sacroiliac joint have done exceedingly well with the suspension sling recommended by Noland and Conwell. Our results in these cases have been eminently satisfactory. When there is marked upward or downward displacement of the fragments, as in the Malgaigne type of fracture or in a fracture of the acetabulum, we have used Russell traction applied to the affected side. We recommend this especially for acetabular fracture, results being exceptionally good. Russell traction, however, should not be used if there is renal infection as indicated by the presence of pus in the urine and elevation of temperature, for the position of the body with the foot of the bed elevated is not

conducive to drainage of the kidneys. In all cases in our service cystograms are now taken as a routine. This enables us to diagnose a rupture of the bladder while there are still extremely few clinical manifestations. In the presence of vesical injury immediate laparotomy is performed. In the presence of urethral injury our first concern is that there shall be no extravasation of urine. Further operative procedures then depend

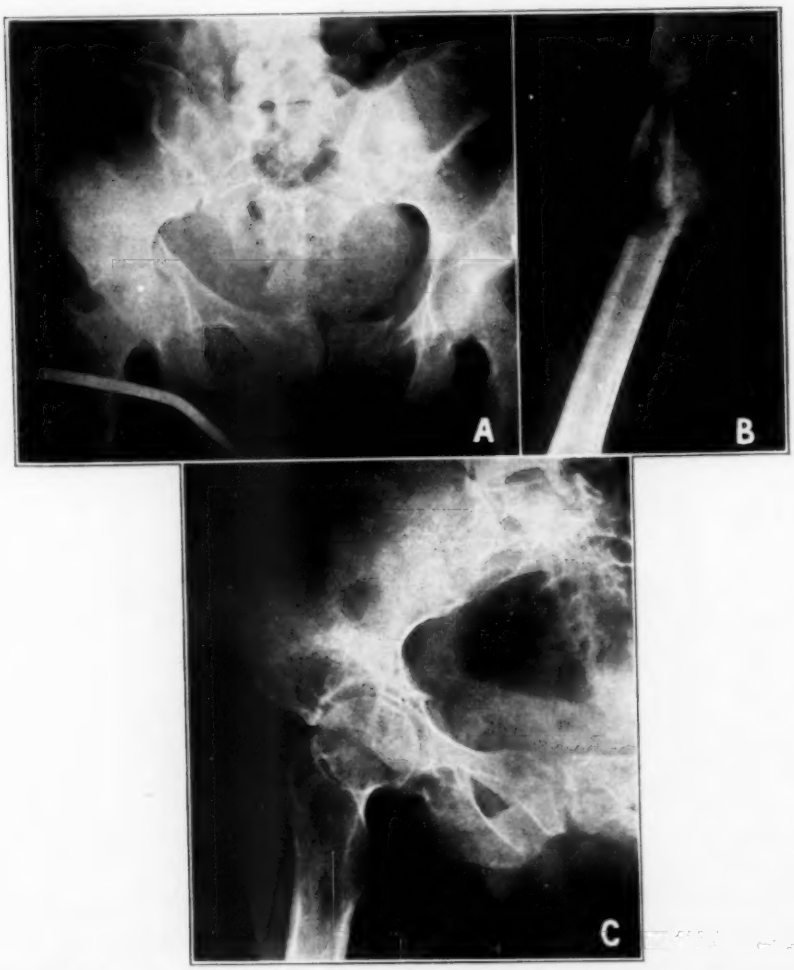

Fig. 6.—Roentgenograms in the case of patient I. B. (table 7). *A*, fracture of the acetabulum. *B*, fracture of the femur. *C*, roentgenogram taken after treatment with Russell traction.

on the patient's general condition. With proper drainage the repair of the urethra may be delayed until the patient has recovered from shock and is able to withstand operation. Shock itself is combated in the usual manner by the use of warm blankets, morphine, venoclysis and other procedures for relief of symptoms.

REVIEW OF LITERATURE

In the following pages we shall give a "highlight review" of the treatment of fractures of the pelvis for the past ten years.

Noland and Conwell [2] report 125 cases, with a mortality of 16 per cent. They describe in detail the overhead pelvic suspension frame. Their usual procedure is traction and suspension for about forty-two days, followed by application of a pelvic belt. They report operative intervention to replace fragments in 2 cases. In 1933, the same authors [3] reported 60 new cases in addition to the previous 125. The mortality for the entire 185 cases was 16.2 per cent; 19 patients died within twenty-four hours. The average stay in the hospital was fifty-three days, and the ratio of male to female patients was 3 to 1. The authors used their customary treatment with the pelvic suspension frame, traction being applied on both lower extremities with abduction of 15 to 20 degrees. They emphasize the use of the spreader to prevent too great a lateral pressure. They use roentgen evidence of callus formation to determine the time at which weight bearing may be permitted. Noland [4] advocates painstaking examination, minimal handling, examination by means of a portable x-ray apparatus and, if necessary, catheterization to obtain a specimen of urine. He advocated waiting several hours before injecting opaque fluids to determine whether the bladder is intact. (It has not been our custom to wait.) His method involves suspension by a canvas sling from the upper third of the thigh to the lower dorsal region. Countersuspension depends on the weight of the parts supported. Suspension is supplemented in every case by traction on the legs and thighs. No traction is used for fracture of the anterior superior or the inferior spine, but simply suspension plus flexion at the knees by means of a pillow. The wooden spreader is also used except when there is separation of the symphysis pubis. In ordinary cases this treatment is continued for forty-two days. The apparatus is removed and a belt applied; the patient is then allowed to remain in bed one more week. He is out of bed by the seventh or eighth week and is allowed to bear weight, using crutches. Hot tub baths and local heat, electrotherapy, hydrotherapy and massage are used during this time. Noland makes the important note that while anatomic position was good in only 55 per cent, functional results were good in most cases.

Koster and Kasman [5] describe an apparatus devised by them, which they have used in 14 cases. Its special recommendation is that the patient

2. Noland, P. L., and Conwell, H. E.: Acute Fractures of the Pelvis, J. A. M. A. **94**:174 (Jan. 18) 1930.

3. Noland, L., and Conwell, H. E.: Fractures of the Pelvis, Surg., Gynec. & Obst. **56**:522 (Feb.) 1933.

4. Noland, L.: Fractures of the Pelvis, Am. J. Surg. **38**:608 (Dec.) 1937.

5. Koster, H., and Kasman, L. P.: Treatment of Fractures of the Pelvis, J. Bone & Joint Surg. **19**:1130 (Oct.) 1937.

is immediately relieved of pain on motion. This apparatus is used for fracture involving the pelvic girdle in which displacement is to be corrected. These authors state, however, that if the displacement can be corrected by traction this should also be applied. (We have not felt it necessary to use this specially devised apparatus.)

Rankin [6] reports 449 cases. He recommends that the treatment be fitted to each individual case, the treatment recommended in the majority of cases being extension of the lower extremities with some form of pelvic sling. He is a strong advocate of immediately using the various forms of physical therapy, concluding that if used early such measures shorten the period of hospitalization.

Kreuscher [7] reports 185 cases. Essentials of his treatment are complete relaxation on a Bradford frame, traction on the lower extremities and overhead suspension. He states that open operation is rarely indicated and that he does not care for the circular plaster cast but immobilizes his patients for six to ten weeks. (We have never found it necessary to use the Bradford frame nor traction on both lower extremities. We, also, have had no use for the circular cast.)

Cubbins' [8] experience has been that the average fracture of the pelvic ring involving the rami of the pubis and ischium with little or no displacement will return to perfect form and function in about twelve weeks, five to seven weeks being spent by the patient in bed without any particular dressing; the patient may be "up and around" under treatment for the succeeding three to five weeks. With wide separation, the patient is suspended in a sling. Moleskin adhesive tape may be used below the iliac crest and over the greater trochanters. The patient may also be suspended in a hammock attached to a Balkan frame. Supports of this hammock may be crossed to give greater lateral pressure. For upward dislocation of one side of the pelvis, traction of 50 to 75 pounds (22 to 34 kg.) on the well limb is applied, with counterpull by means of a belt beneath the opposite tuberosity of the ischium. If this is not successful, Cubbins suggested the use of the Hawley table with extension by screw traction. For acetabular fracture he uses lateral traction with a band around the thigh in addition to longitudinal traction. In some cases he has used a large screw driven into the neck of the femur, lateral traction being applied to this. For fracture of the acetabulum in which the fragments are locked he does an open operation to extract the head of the femur.

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6. Rankin, L. M.: Fractures of the Pelvis, Ann. Surg. **106**:266 (Aug.) 1937.

7. Kreuscher, P. H.: Fractures of the Pelvis, Indust. Med. **5**:185 (April) 1936.

8. Cubbins, W. R.: Fractures of the Pelvis, Northwest Med. **35**:63 (Feb.) 1936.

Billington [9] in his cases of simple fracture orders rest in bed with an adhesive plaster swathe. He also uses a pelvic binder of elastic stockinet held in place by perineal straps. For more severe fracture the pelvic hammock and bilateral leg traction, as described by Conwell, are used.

Weil, Henry and Rusbridge [10] report 228 cases. They give an excellent exposition of the initial treatment of this type of fracture and stress the treatment of the injured bladder. They insist that rectal examination must not be overlooked. They like the hammock suspension of Conwell. Their patients are usually confined to bed for eight to ten weeks. In their series of cases the mortality was 12.2 per cent, and the period of disability averaged one hundred and forty-eight and two-tenths days.

Langan [11] reports 40 cases and describes the use of the Jones splint. (We have never had recourse to the use of this splint.) Langan manipulates the fragments through the vagina and rectum. (This has never been done in any of our cases.) However, in the article referred to Langan does not distinguish between the sites of fractures of the neck of the femur, and it is therefore hard to evaluate the value of the splint from the evidence presented.

Haggart [12] uses the pelvic swathe for fracture complicated by visceral injuries. His method closely follows that of Conwell. In an occasional case he uses plaster boots applied to both legs and connected by a cross member. (This method has never been used by us.)

Papik [13] advocates the use of a Jones and Anderson splint to obtain simultaneous traction and abduction for central dislocation of the head of the femur. The legs must be placed in a cast in which the apparatus is incorporated. (This method has never been necessary in our cases. We feel that Russell traction is more effective and more comfortable.)

McBride [14] describes an apparatus for traction and fixation which allows the patient to be raised and lowered without disturbing the traction. (Again, we have felt that Russell traction answers the purpose very well.)

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9. Billington, R. W.: Fractures of the Pelvis, J. Tennessee M. A. **28**:453 (Nov.) 1935.

10. Weil, G. C.; Henry, J. P., and Rusbridge, H. W.: Treatment of Fractures of the Pelvis, Pennsylvania M. J. **38**:942 (Sept.) 1935.

11. Langan, A. J.: Use of the Jones Splint in Treatment of Fractures of the Pelvis, J. Bone & Joint Surg. **17**:435 (April) 1935.

12. Haggart, G. E.: Fractures of the Pelvis, S. Clin. North America **14**:1197 (Oct.) 1934.

13. Papik, C.: The Management of Pelvic Fractures, Internat. J. Med. & Surg. **47**:78 (Feb.) 1934.

14. McBride, E.: The Underslung Traction Saddle Frame in Fractures of the Pelvis, Ann. Surg. **97**:309 (Feb.) 1933.

Henson and Lublin [15] report 112 cases. Their patients are strapped tightly with adhesive tape. Traction is not used. Plaster casts have been used in 12 per cent of the cases. The average stay in the hospital is twenty-three and one-half days. No attempt is made to obtain perfect anatomic position.

Gilmour [16] cites 81 cases. In his article he lays particular stress on the diagnosis of rupture of the bladder.

Leadbetter [17] reports 100 cases, 80 per cent of the patients being female. His method of treatment is related to the suspension and traction apparatus, including use of the Balkan frame, the Thomas splint and fixation with adhesive tape. When the fragments do not move in forty-eight hours he uses skeletal traction by pins or tongs. (We have never found it necessary to do this.) Traction is maintained in his cases for six weeks, and weight bearing is allowed at the tenth week. Open operation is performed only for overriding fracture of the pelvic bones. In a discussion of his article much is made of the Maxwell-Ruth lateral traction method, which we have never found necessary.

Rutherford [18] reports about 200 cases without a fatality. His patients are placed on a level traction bed and allowed to move about. He rarely uses traction or a plaster cast.

Jones and Buckner [19] report 40 personal cases and 312 other cases. The mortality in the former series was 2.5 per cent and in the latter 15 per cent. For fractures of the iliac wing they use a well fitting body cast. For fracture involving the acetabulum they have used the Whitman spica with 20 per cent abduction of the leg, allowing the cast to remain in place for twelve weeks. Forward displacement of half the pelvis is treated by skeletal traction by means of ice tongs applied just above the condyles of the femur. When there is lateral spreading they use suspension with a wide canvas band, the suspending ropes being crossed. For separation of the symphysis pubis they perform a wiring operation. (The last named we have not needed, as the pelvic sling produces the desired results.)

Martin [20] describes a belt which he has used in 5 cases, with satisfactory results.

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15. Henson, E. B., and Lublin, R. D.: Fractures of the Pelvis, West Virginia M. J. **28**:539 (Dec.) 1932.

16. Gilmour, W. R.: Acute Fractures of the Pelvis, Ann. Surg. **95**:161 (Feb.) 1932.

17. Leadbetter, G. W.: Fractures of the Pelvis, South. M. J. **25**:742 (July) 1932.

18. Rutherford, A. G.: Management of Fractures of the Pelvis, West Virginia M. J. **27**:298 (July) 1931.

19. Jones, E. O., and Buckner, H. T.: Fractures of the Pelvis, Northwest Med. **30**:269 (June) 1931.

20. Martin, E. D.: A New Bandage for Treatment of Fractures of the Pelvis, New Orleans M. & S. J. **83**:678 (April) 1931.

Todd [21] reports 47 cases, with 3 deaths. He advises the use of a Bradford frame, with strapping or a binder about the pelvis. This is then replaced with a light plaster cast. The patient is kept in bed one month. He cites a case in which he used heavy traction and suspension. Michel [22] uses the Bradford frame with the knee flexed on a pillow and a broad encircling band of adhesive tape around the pelvis. When conditions indicate it he also uses pelvic suspension with a spreader and traction on the lower extremities.

Parker [23] cites 19 pelvic fractures with a mortality of a little more than 10 per cent. In most cases he uses simple rest in bed with the patient flat on the back, sand bags providing support for the legs and pelvis. In case of displacement he uses traction and abduction. For fracture of the acetabulum he formerly used traction followed by application of a plaster cast. This was found unsatisfactory, and he now uses the overhead frame with suspension and extension. His article contains a good discussion of vesical and renal injuries.

Brooksher [24] reports 25 cases, with a mortality of 12 per cent. In the majority of his cases he has used strapping with adhesive plaster. He has also used Buck's extension plaster cast and the Bradford frame. Open operation is not performed.

Herzikoff [25] describes an apparatus which uses the sling and suspension for fracture of the pelvis with wide separation of fragments, especially in the region of the symphysis pubis. He condemns the swathe, the plaster spica, the Bradford frame and the Thomas splint.

McNealy and Willems [26] report 30 cases, the average period of hospitalization being ninety-five days. For forward displacement they use an extension apparatus. For pubic fracture with overriding they manipulate the fragments vaginally or rectally. They also use a plaster of paris cast extending from the umbilicus to the midthigh, putting a cross bar between. For disturbance of the acetabulum they use the Whitman method and the method of Putti, which is the insertion of a steel pin through the trochanter and the application of traction. (It has never

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21. Todd, M. H.: Fractures of the Pelvis, Virginia M. Monthly **57**:781 (March) 1931.

22. Michel, H. M.: Fractures of the Pelvis, South. M. J. **24**:263 (March) 1931.

23. Parker, O. W.: Fractures of the Pelvis, Minnesota Med. **14**:29 (Jan.) 1931.

24. Brooksher, W. R.: Fractures of the Pelvis, J. Arkansas M. Soc. **26**:242 (May) 1930.

25. Herzikoff, S.: Apparatus Used in Treatment of Fractures of the Pelvis, California & West. Med. **32**:253 (April) 1930.

26. McNealy, R. W., and Willems, J. D.: Fractures of the Pelvis, Am. J. Surg. **8**:573 (March) 1930.

been our policy to manipulate fragments either rectally or vaginally or to use the Whitman spica.)

Colp and Findlay [27] review 35 cases. Practically the only treatment which they render is rest in bed for about thirty days. The patient is allowed to walk on about the thirty-eighth day. They have also used pelvic strapping and elastic belts. They report 1 case of unsuccessful treatment with the Balkan frame and traction to bring down a posterior displacement of the ilium. They do not resort to operation or to casts.

Boorstein [28] reports on 100 cases. His favorite method is to use the Bradford frame, with strapping adhesive plaster and lacing in front. For upward displacement he applies extension of both limbs by weights and pulleys or by the Thomas Jones brace.

Bates [29] remarks that the two essentials of treatment are reduction and immobilization. For a broken iliac crest or ramus he uses replacement by pressure or manipulation and retention by pads and adhesive tape. For simple fracture with intrapelvic damage, extension of both lower limbs with abduction of the hips and elevation of the foot of the bed are used. For pelvic fracture associated with fracture of the thigh he uses the Hodgen splint. He discusses in detail the Murphy sling for the handling of any type of pelvic fracture.

Wakeley [30] reports 100 cases. For fracture of the whole pelvic girdle (44 cases reported) he uses a broad binder for ten days and then a cast for six weeks. The patient is allowed to be up on crutches in nine weeks. For fracture of the ilium (18 cases reported), the os pubis (24 cases reported) and the sacrum (4 cases reported) the treatment is the same. For fractures of the ischium (5 cases reported) therapy consists of rest in bed for six weeks. For fracture of the acetabulum (2 cases reported) extension is used for two weeks, followed by immobilization in plaster for six weeks. For fracture of the coccyx (3 cases reported) he manipulates the fragments through the rectum and prescribes rest in bed.

Holderman [31] discusses only pelvic fracture with separation of the symphysis pubis. He does not use the swathe or strapping with adhe-

27. Colp, R., and Findlay, R. T.: Fractures of the Pelvis, Surg., Gynec. & Obst. **49**:847 (Dec.) 1929.

28. Boorstein, S. W.: Fractures of the True Pelvic Ring, Am. J. Surg. **7**: 633 (Nov.) 1929.

29. Bates, T. H.: Fractures of the Pelvis: Treatment by Murphy Sling, J. Florida M. A. **16**:68 (Aug.) 1929.

30. Wakeley, C. P. G.: Fractures of the Pelvis, Brit. J. Surg. **17**:22 (July) 1929.

31. Holderman, H. H.: Fractures of the Pelvis with Separation of the Symphysis Pubis, Pennsylvania M. J. **32**:16 (Oct.) 1928.

sive tape. However, he does describe a belt with a buckle, which is passed over and around the pelvis with the patient on a Bradford frame.

Sever [32] reports 51 cases, with 1 death. This article contains a good review of the literature. He concludes that acetabular fracture is the most disabling and advises that the Whitman abduction method or the method of Putti [33] be used. For fracture of the ilium or pubic arch he uses rest in bed with a tight swathe. Occasionally he makes use of a pelvic sling. For fracture of the pubic arch, the sacroiliac joint and the wing of the ilium, with displacement, he makes use of traction on the leg combined with a pelvic swathe.

Wilson [34] competently discusses vesical and urethral injuries. He applies a plaster cast for the pelvis and both thighs, leaving this in place for two to three months. No weight bearing is permitted for one month after the cast is removed. He advocates the use of silver wire to bring together separated pubic bones. For acetabular fracture he immobilizes the joint in plaster for two months, with moderate abduction of the thigh. When the head of the femur is driven through the acetabulum he uses a hook above the greater trochanter with manipulation through the vagina or rectum to replace the fragments and then immobilizes the pelvis in plaster with full abduction.

Furniss [35] reports 20 cases with good results irrespective of the treatment employed. He uses on occasion rest in bed, a girdle of adhesive tape 2 inches (5.08 cm.) wide or sand bags to the outer side of the thighs. He also uses manual reposition of the fragments. He commends suspension and traction.

(An apparatus has recently been described; it is called the Brendel symphysis reduction tractor. By means of two hooks inserted into each obturator foramen, the separated symphysis may be brought together and wired. The tractor is then removed. We have had no experience with this apparatus.)

ANALYSIS OF DEATHS

There were 14 deaths in our series of 79 cases, a percentage of 17.7 per cent. Nine patients died within six hours. Following is a brief report of the cases in which death occurred. The patients in cases 1 to

32. Sever, J. W.: Fracture of the Pelvis, New England J. Med. **199**:16 (July 5) 1928.

33. Putti, V.: Sulla terapia della lussazione centrale del femore, Chir. d. org. di movimento **11**:530 (Aug.) 1927.

34. Wilson, G. E.: Fractures of the Pelvis, St. Michael's Hosp. M. Bull. **3**:56 (Dec.) 1927.

35. Furniss, J. N.: Fractures of the Pelvis, Internat. J. Med. & Surg. **40**: 344 (Aug.) 1927.

5, inclusive, lived over six hours after injury; those in cases 6 to 14, inclusive, died within six hours.

CASE 1.—E. B., a man aged 23, had a gunshot wound in the pelvic region. Roentgen examination revealed a perforating fracture of the left ilium, the ascending ramus of the left pubic bone and the sacrum near the sacroiliac articulation. The bladder was also perforated. Operation was performed immediately to close the vesical perforations. Peritonitis developed, and the patient died four days later.

CASE 2.—J. J., a man aged 25, fell down a flight of ten steps. The right ilium was fractured, with no associated injury. The patient died on the third day. The postmortem diagnosis was fracture of the pelvis and hypostatic pneumonia.

CASE 3.—H. J., a man aged 58, jumped from a third story window. He received a fracture of the lateral mass on the left side of the sacrum and a fracture of the descending ramus of the left pubic bone. He also had fractures of the transverse processes of the fourth and fifth lumbar vertebrae. Infection of the urinary tract developed, and the patient died fourteen days later. He was not catheterized during his stay in the hospital.

CASE 4.—J. J., a woman aged 28, jumped four stories from a window. Roentgenograms showed comminuted fractures of the ascending and descending rami, the right pubic bone, the right acetabulum and the right ilium. There were associated injuries, consisting of the following: fracture of the right transverse processes of the fifth lumbar vertebra; fracture of the coccyx; fracture of the tibia and the fibula, and fracture of several metacarpal bones. This patient survived for sixty-two hours.

CASE 5.—W. B., a man aged 24, was struck by an automobile. The pelvis showed fractures of the right and the left pubic bone, extending into the left acetabulum. In association with these there were subarachnoid hemorrhage, rupture of the bladder and the membranous portion of the urethra and laceration of the prostate and the anterior wall of the rectum. This patient lived eleven hours and was reported by the medical examiner as having died of shock and retroperitoneal hemorrhage.

CASE 6.—F. M., a man aged 28, was found lying in the street. The cause of the pelvic fracture was unknown. Fracture of the left ilium, the left acetabulum and the decending ramus of the left pubic bone was present. In addition, there were fractures of the left femur, the right femur and the right humerus. There was also an intracranial injury. The patient died four hours after his admission to the hospital. The postmortem diagnosis was multiple fracture associated with laceration of the liver.

CASE 7.—R. T., a man aged 26, jumped from a window. Roentgen examination revealed a separation of the symphysis pubis and a compound fracture of the right ankle. The patient lived one hour. The postmortem diagnosis was fractures of the pelvis and the right leg, with shock.

CASE 8.—C. V., a boy aged 15, was caught between two "L" cars. There were fracture of the descending ramus of the right pubic bone and also fracture of right radius, the right ulna, the right femur and the right tibia. The patient lived six hours. The postmortem report corresponded with the clinical findings.

CASE 9.—An unidentified Negro had a fracture of the ascending and descending rami of the left pubic bone and the outer part of the left side of the sacrum, near the acetabulum. He also had a comminuted fracture of the upper third of the

TABLE 8.—*Analysis of Deaths*

TABLE 8.—*Analysis of Deaths*

Patient	Age	Sex	Cause of Pelvic Fracture	Type of Injury	Associated Injuries	Time in Hospital	Cause of Death
E. B.	23	M	Gunshot	Perforating fracture of left ilium, left ascending ramus of pubic bone and sacrum near left sacroiliac articulation	Perforation of bladder	4 days	Peritonitis
J. J.	25	M	Fell 10 steps	Fracture of right ilium	None	5 days	Postmortem diagnosis, fracture of pelvis; hypostatic pneumonia
H. H.	58	M	Jumped from 3d story window	Fracture of lateral mass of left side of sacrum and descending ramus of left pubic bone	Fracture of transverse processes of 4th and 5th left lumbar vertebrae	14 days	Infection of urinary tract
F. M.	28	M	Unknown	Fracture of left ilium, left acetabulum, descending ramus of right pubic bone	Fracture of left femur, right femur, right humerus; intracranial injury	4 hr.	Multiple fractures; lacerations of liver
R. T.	26	M	Jumped from window	Separation of symphysis pubis	Compound fracture of right ankle	1 hr.	Postmortem diagnosis, fracture of pelvis and right leg; shock
C. V.	15	M	Caught between "L" cars	Fracture of descending ramus of right pubic bone	Fracture of right radius, right ulna, right femur and right tibia	6 hr.	Postmortem diagnosis same as clinical findings
U. C. M.	?	M	Unknown	Fracture of ascending and descending ramus of left pubic bone and outer part of left side of sacrum, near acetabulum	Comminuted fracture of left femur, extending into intertrochanteric region	1½ hr.	Multiple fractures; shock
U. C. M.	32	M	Fell from window	Multiple fractures of pelvis	Multiple fractures of long bones	5 min.	Multiple fractures; shock
L. R.	20	M	Jumped 5 stories	Compression fracture of sacrum and dislocation of both sacroiliac joints	Fracture of 12th dorsal and 1st lumbar vertebral bodies; fracture of transverse process of 5th lumbar vertebra	2 hr. 10 min.	Shock; internal injuries; multiple fractures
E. J.	27	M	Fell from 3d story window	Fracture of body of right pubic bone	Fracture of skull; laceration of brain; fractures of 2d to 9th right ribs; laceration of right kidney; puncture of chest and heart	4 hr. 25 min.	Postmortem diagnosis same as clinical findings
J. J.	28	F	Jumped 4 stories	Comminuted fracture of ascending and descending rami of right pubic bone; fracture of acetabulum; fracture of right ilium	Fracture of transverse process of right and left 5th lumbar vertebrae; fracture of coccyx; fracture of tibia and fibula	62 hr.	Died
W. B.	24	M	Struck by automobile	Fracture of right and left pubic bone and left acetabulum	Shock; retroperitoneal hemorrhage; ruptured bladder	11 hr.	Died
B. H.	43	M	Unknown	Fracture of crest of left ilium	Fracture of spinous process down dorsolumbar portion of spine	3 hr.	Died
A. B.	27	F	Fell 3 stories	Fracture of pubic bones; fracture of acteabulum	Fracture of lower end of right humerus and of right ulna; injury to bladder and spleen	6 hr.	Died

left femur, extending into the intertrochanteric region. The patient lived one and one-half hours. The cause of death was reported as multiple fractures and shock.

CASE 10.—An unidentified Negro aged 32 was admitted to the hospital after falling from a window. There were multiple fractures of the pelvis and multiple fractures of the long bones. The patient lived five minutes. The cause of death was reported as multiple fractures and shock.

CASE 11.—L. R., a man aged 20, jumped from the fifth story of a house. A compression fracture of the sacrum and dislocation of both sacroiliac joints occurred. There were also fractures of the bodies of the twelfth dorsal and the first lumbar vertebra and a fracture of the right transverse process of the fifth lumbar vertebra. The patient lived two hours and ten minutes. The cause of death was reported as multiple fractures, and shock.

CASE 12.—E. J., a man aged 27, fell from a third story window. The body of the right pubic bone was fractured. There were also fracture of the skull with laceration of the brain, fractures of two to nine right ribs and lacerations of the right kidney. The postmortem report corresponded with the clinical findings.

CASE 13.—B. H., a man aged 43, was injured in an unknown manner. The pelvic fracture consisted of a fracture of the crest of the left ilium. The associated injuries included fractures of the spinous processes of the lower dorsal, the lumbar and the sacral vertebrae. The cause of death as reported by the medical examiner was fracture of the pelvis and retroperitoneal hemorrhage. The man lived three hours.

CASE 14.—A. B., a woman aged 27, fell three stories from a window. Bilateral fracture of the pubic bone into the right acetabulum occurred. In addition, there were fractures of the right humerus and ulna, rupture of the spleen and rupture of the bladder. The patient lived six hours.

SUMMARY AND CONCLUSIONS

1. Cystograms are of inestimable value in the diagnosis and treatment of pelvic fractures and associated conditions.

2. A simple method of treatment is preferable to a complicated procedure.

3. Treatment should never be a matter of routine but should be adopted to each case.

4. Concomitant pathologic conditions of the genitourinary tract must be carefully searched for.

5. Neurologic examinations must be made in every case.

6. Pelvic fracture with associated injuries is not infrequent. The latter must be constantly sought for.

FATAL PULMONARY EMBOLISM

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The frequency of sudden death from massive pulmonary embolism in the patient who has successfully passed through a major surgical operation or is recuperating from an injury, the recent parturient and the person with cardiac disease or phlebitis warrants a consideration of this condition.

The incidence of fatal pulmonary embolism may be seen from the following figures:

		Percentage
Belt [1] (Toronto)	567 autopsies (med. : surg. :: 40 : 16)	6.5
McCartney [2] (Minnesota)	14,419 autopsies 9,615 medical deaths (1.89%) 2,139 traumatic deaths (3.32%) 2,331 postoperative deaths (5.10%) 284 postpartum deaths (5.28%)	2.72
Collins [3] (Los Angeles)	10,940 autopsies	2.07
Russum and Kemp (Omaha)	1,781 autopsies	1.34
Yearly deaths in United States	33,748 (Barnes [4])	
Persons alive now who will die of embolism,	3,068,000 (Barnes [4])	

In our own small series, the basis of this communication, 5 deaths were post-traumatic, 5 followed medical treatment, 13 were postoperative and 1 was postpartum. The cases were observed in 1,781 consecutive unselected autopsies on adults from Jan. 1, 1926, to Oct. 31, 1937. The material came from general hospitals and from the coroner's service.

A study of our own material and a survey of the literature indicate the importance of the following three points:

1. The increased risk of this complication for certain persons and with certain types of operation.

From the Department of Pathology, the Creighton University School of Medicine.

1. Belt, T. H.: Thrombosis and Pulmonary Embolism, Am. J. Path. **10**:129-144 (Jan.) 1934.

2. McCartney, J. S., cited by Barnes.[4]

3. Collins, D. C.: Pulmonary Embolism Based upon a Study of Two Hundred and Seventy-One Instances, Am. J. Surg. **33**:210-219 (Aug.) 1936.

4. Barnes, A. R.: Pulmonary Embolism, J. A. M. A. **109**:1347-1353 (Oct. 23) 1937.

2. The advantage of recognizing nonfatal pulmonary embolism and the premonitory signs of fatal embolism.

3. The possibility of preventing the condition and of emergency surgical intervention when embolism has occurred and death is not immediate.

APPRECIATION OF RISK OF EMBOLISM

The influence of age, sex, type of operation, cardiac disease and obesity must be considered for individual patients.

Age.—Age is a predisposing factor. In our series the youngest patient was 34 and the oldest 68. Barker [5] reviewed the deaths at the Mayo Clinic following surgical operations from 1928 to 1933 and found that in the cases in which autopsy was done 93 per cent of embolisms were in persons over 40 years of age and 70 per cent in those over 50. Robertson [6] stated that the clinical histories in such cases are similar in that the age incidence is over 30 years. Vance,[7] in 60 deaths from embolism following trauma, found an age incidence of 30 to 80, with an average of 55. Henderson [8] in 1927 reviewed the autopsy records of the Mayo Clinic for the preceding ten years and found the average age at death from pulmonary embolism to be 53.2, which is 10.4 years greater than the average age of patients operated on there. These figures indicate that the danger of embolism is slight before the age of 30 and increases sharply after 40.

Cardiac Disease.—In 13 of our 24 cases some type of cardiac disease was demonstrated at autopsy. In all of our medical cases the heart was damaged.

In various series of fatal embolisms cardiac disease has a high incidence. In Belt's [1] cases 84 per cent of patients had impaired cardiac function.

The age distribution and cardiac involvement in our series was as follows:

31-40	5 cases	(2 postoperative, 3 medical) Cardiac involvement—2 medical.
41-50	9 cases	(6 postoperative; 1 medical; 1 traumatic; 1 puerperal) Cardiac involvement—2 postoperative; 1 medical.
51-60	5 cases	(3 traumatic; 1 medical; 1 postoperative) Cardiac involvement—1 medical; 1 traumatic; 1 postoperative.
61-70	5 cases	(4 postoperative; 1 traumatic) Cardiac involvement—all cases.

5. Barker, N. W., cited by Barnes.[4]

6. Robertson, H. E.: Pulmonary Embolism Following Surgical Operation, Am. J. Surg. **26**:15-18 (Sept.) 1934.

7. Vance, B. M.: Thrombosis of the Veins of the Lower Extremity and Pulmonary Embolism as a Complication of Trauma, Am. J. Surg. **26**:19-26 (Oct.) 1934.

8. Henderson, E. F.: Fatal Pulmonary Embolism: A Statistical Review, Arch. Surg. **15**:231-236 (Aug.) 1927.

Sex.—The incidence of embolism is somewhat higher in the female sex, according to most writers. In our cases the sex distribution is the reverse of that encountered in any large series, as 15 of our patients were men and 9 were women. Henderson found death due to embolism in 223 patients, 104 men and 119 women. In Vance's 60 cases of post-traumatic embolism there were 37 female and 23 male patients. In 1927 McCartney [9] examined 9,225 necropsy records at the University of Minnesota and noted 73 deaths due to embolism, occurring in 40 males and 33 females. He stated that sex plays no important role. Later the same author [10] made an additional study of the autopsies from 1927 to 1933 and observed a significant difference in the incidence of embolism after trauma in the male and in the female. In the male it was 2.8 per cent and in the female 8.6 per cent. Differences in age did not explain the variation, while the incidence of coinicident cardiac disease was even higher in males. Although unable to demonstrate the fact in his cases, McCartney suggested that probably the higher incidence of varicose veins in women explains the greater incidence of embolism.

Type of Operation.—Consideration of the type of operation is most important in estimating the danger of embolism in surgical cases. In our series the incidence was as follows: prostatectomy, 3; varicose vein resection, 1; gastroenterostomy, 1; cholecystectomy, 1; herniotomy, 3; hysterectomy and appendectomy, 1; resection of rectum, 1; appendectomy, 1; salpingo-oophorectomy, 1, and thoracotomy, 1.

Barker [5] reported the frequency of postoperative embolism at the Mayo Clinic for the period from 1928 to 1933 greatest after the following operations, in descending order of frequency: exploratory laparotomy for inoperable malignant tumor, colostomy, enterostomy, femoral or inguinal herniotomy, resection of the intestine, hysterectomy, operation for ruptured appendix, operations on the prostate and urinary bladder, open reduction of fracture, operations on the brain and the spinal cord and cholecystectomy.

Most postoperative emboli are preceded by abdominal operations. Numerous studies are available in this connection. Henderson found only 43 cases of fatal embolism following extra-abdominal operations. In the group were 14 operations for hernia and 8 operations on the breast.

Embolism after operations on the abdomen or the pelvis seems to result from interference with the circulation in the lower extremities,

9. McCartney, J. S.: Pulmonary Embolism, Arch. Path. **3**:921-937 (June) 1927.

10. McCartney, J. S.: Pulmonary Embolism Following Trauma, Surg., Gynec. & Obst. **61**:369-378 (Sept.) 1935.

favoring the development of thrombosis in veins there. Slowing of the circulation alone probably does not cause thombosis, but experience shows that thrombosis develops in regions where the circulation is slow, that is, in the veins of the lower extremities and in the auricular appendages of the heart. The circulation in the veins is maintained by the drive of the arterial circulation, contraction of the skeletal muscles, negative intrathoracic pressure in inspiration and the plunger-like action of the liver in squeezing blood out of the abdomen. Operations on the abdomen tend to disturb this venous circulation. The blood pressure is apt to fall, especially if there is cardiac disease. The patient lies quietly on his back for many days, and the legs are not moved, so that muscular contractions no longer help the venous blood to return to the abdomen. Because of pain, bandages and adhesive tape the abdomen is quiet and the respiratory excursions are shallow. As a result, the suction action of the changes in the intrathoracic pressure and the plunger action of the liver are reduced to a minimum. It has been shown by Blumgart and Weiss [11] that in the presence of cardiac insufficiency the circulation time is prolonged, the velocity of venous return flow is reduced and the veins of the lower extremity suffer first.

In addition to slowing of the circulation, other factors probably instrumental in producing postoperative thrombosis are increase in the number of blood platelets, liberation of increased amounts of tissue juices into the circulation and a return to a full diet with increased protein intake.

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11. Blumgart, H. L., and Weiss, S.: Clinical Studies on the Velocity of Blood Flow: II. The Velocity of Blood Flow in Normal Resting Individuals, and a Critique of the Method Used, J. Clin. Investigation **4**:15-31 (April) 1927; III. The Velocity of Blood Flow and Its Relation to Other Aspects of the Circulation in Patients with Rheumatic and Syphilitic Heart Disease, ibid. **4**:149-171 (June) 1927; IV. The Velocity of Blood Flow and Its Relation to Other Aspects of the Circulation in Patients with Arteriosclerosis and in Patients with Arterial Hypertension, ibid. **4**:173-197 (June) 1927; V. The Physiological and the Pathological Significance of the Velocity of Blood Flow, ibid. **4**:199-209 (June) 1927; VI. The Method of Collecting Active Deposit of Radium and Its Preparation for Intravenous Injection, ibid. **4**:389-398 (Aug.) 1927; VII. Pulmonary Circulation Time in Normal Resting Individuals, ibid. **4**:399-425 (Aug.) 1927; VIII. Velocity of Blood Flow and Its Relation to Other Aspects of the Circulation in Patients with Pulmonary Emphysema, ibid. **4**:555-574 (Oct.) 1927; IX. The Pulmonary Circulation Time, the Velocity of Venous Blood Flow to the Heart, and Related Aspects of the Circulation in Patients with Cardiovascular Disease, ibid. **5**:343-377 (Feb.) 1928; X. The Relation Between the Velocity of Blood Flow, the Venous Pressure and the Vital Capacity of the Lungs in Fifty Patients with Cardiovascular Disease Compared with Similar Measurements in Fifty Normal Persons, ibid. **5**:379-392 (Feb.) 1928.

Thrombosis begins with a deposit of blood platelets on the vessel linings. Brock [12] discussed the increased platelet count observed after operations and post partum and noted that the peak of this count was reached at about ten days, corresponding with the usually observed occurrence of thrombosis.

Galloway [13] noted that the platelets increased up to 180 per cent in 10 cases in which embolism followed fracture.

Perhaps the only common factor in the occurrence of all thromboses is the liberation of increased amounts of tissue juices into the circulation. Pickering and Mathur [14] found that the ingress of tissue juices into the circulation induces hypercoagulability and later an increase of platelets but does not suffice for the inception of thrombosis. Both factors are important in the inception or growth of thrombi when the condition of the blood plasma favors the deposition and clumping of the platelets or when the stability of plasma colloids is reduced.

The influence of diet on the agglutinability of platelets has been noted by Pickering and Mathur. This agglutinability is much less after a meal of carbohydrates than after one of meat. Mills [15] reported that in postoperative, postfebrile and postpartum conditions the platelet count, which has been sharply decreased in pregnancy or fever, begins to rise. It reaches a peak on the eighth to the eleventh day after the fever subsides or after delivery. It then returns to normal in four or five days. This rise in the platelet count usually occurs when the patient is allowed to be up for mild exercise and when full diet is resumed. The increased protein intake increases the tendency of the platelets to clump and distintegrate.

Obesity.—Pulmonary embolism following operation more often causes death in the obese than in persons of average weight. Snell [16] studied the relation of obesity to postoperative embolism at the Mayo Clinic and concluded that "there is a group of patients over 50 years of age, obese and with normal or subnormal blood pressure, who are particularly susceptible." Eight of the 13 postoperative deaths in our series occured in overweight patients.

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12. Brock, R. C.: Postoperative Venous Thrombosis and the Platelet Count, Lancet **1**:688-690 (April 1) 1933.

13. Galloway, J. F.: The Blood Platelets After Fracture, Lancet **1**:1082 (May 16) 1931.

14. Pickering, J. W., and Mathur, S. N.: Role of Tissue Juices in Thrombosis, Lancet **2**:387-388 (Aug. 20) 1932.

15. Mills, C. A.: Relation of Protein Diet to Thrombosis, Ann. Surg. **91**: 489-491 (April) 1930.

16. Snell, A. M.: The Relation of Obesity to Fatal Postoperative Pulmonary Embolism, Arch. Surg. **15**:237-244 (Aug.) 1927.

In summing up the available data on our first point, the necessity of appreciating the increased risk of pulmonary embolism in certain persons and in certain type of operations, we would stress the following factors:

The patient under 30 runs little risk. The greatest risk is between the ages of 40 and 60.

A woman of susceptible age runs a slightly greater risk of postoperative embolism than does a man. After an accidental injury the risk is three times as great for the female, probably because of the greater incidence of varicose veins.

Operations on the abdomen and the pelvis subject the patient to much greater risk of complicating embolism than do extra-abdominal operations. Exploratory laparotomy for inoperable malignant tumor, colostomy, enterostomy, herniotomy and resection of the intestine carry the greatest danger of this complication.

Disease of the heart increases the threat of embolism because of a failure to maintain efficient circulation.

A patient who is overweight, especially if over the age of 50 and with a normal or subnormal blood pressure, faces a greater risk of embolism.

ADVANTAGE OF RECOGNIZING NONFATAL EMBOLISIM AND PREMONITORY SIGNS OF FATAL EMBOLISM

Recognition of nonfatal embolism suggests extreme caution in subsequent treatment. A more prolonged stay in bed is indicated. The patient should not be allowed even to go to the bathroom. Bowel movements should be facilitated by liquid petrolatum or by enemas.

Postmortem evidence of previous nonfatal embolism was observed in 8 of our cases. The lower lobes of both lungs were the sites of the resulting infarcts in 4 instances, while in each of 3 patients one lower lobe only was involved. The average time of appearance of the embolism for the entire group was five days after the onset of illness.

One will more accurately recognize embolism if shock is the criterion for diagnosis. Cyanosis and dyspnea are not cardinal symptoms. In cases of nonfatal embolism one should look for minor grades of the same symptoms most frequently observed in our fatal cases—perspiration, imperceptible pulse, weakness and pain in the chest. Barnes pointed out that the common picture is "shock, with or without dyspnea, with faintness, pallor, sweating, acceleration of the pulse, a marked fall in blood pressure, vomiting and sometimes collapse." In many instances an infarct will be produced, and the classic signs of rise in temperature, cough, pleural friction rub, roentgenographic signs of pulmonary consolidation and hemoptysis will follow. In some cases, however, no

infarct is produced, as the collateral circulation in the lung is sufficient to care for the embolism. In such a case the shock syndrome in varying degrees makes the diagnosis.

The embolus may be massive but nonlethal. White [17] stated that in this condition the right ventricle and the pulmonary conus dilate, producing pulsation in the second and third left interspaces, with a loud systolic murmur there and an accentuated P wave in lead II. Friction rub and gallop rhythm may be present. The cervical veins may be dilated and pulsing, and extreme cyanosis develops. The roentgenogram may reveal accentuation of the hilus shadow on the occluded side, and Camp [18] stated the opinion that this is due to dilatation of the pulmonary vessels. White,[17] McGinn and White [19] and Barnes [20] reported electrocardiographic changes characteristic of acute pulmonary embolism by which it can be differentiated from coronary thrombosis. Barnes

TABLE 1.—*Symptoms of Fatal Pulmonary Embolism (Twenty-Four Cases)*

15 patients	.....	Sudden death
1 patient	Lived a few moments	Pain in the chest
1 patient	Lived 8 minutes	Tightness in the chest; clammy skin
1 patient	Lived 30 minutes	Cyanosis; imperceptible pulse
1 patient	Lived 35 minutes	Tightness in the chest; weakness
1 patient	Lived 1 hour	Dyspnea; weakness; restlessness
1 patient	Lived 1½ hours	Pain in the chest; slow respirations; cyanosis; imperceptible pulse
1 patient	Lived 2½ hours	Dyspnea; weakness; dizziness; headache
1 patient	Lived 3 hours	Dyspnea; weakness; slight fever; weak pulse
1 patient	Lived 24 hours	Pain in the chest; perspiration

gave reports of 2 cases in which there were mild premonitory and severe sublethal attacks and in which the electrocardiogram was diagnostic.

In our series the average time at which fatal embolism occurred in the postoperative group was sixteen days, while in the post-traumatic group it was forty-one days.

Even though the embolus is massive and lethal, death does not always occur at once, as our cases indicate (table 1).

The most common symptoms and signs are perspiration, imperceptible pulse, weakness and pain in the chest.

The next most common symptoms and signs are a tight feeling in the chest, dyspnea and cyanosis.

17. White, P. D.: The Acute Cor Pulmonale, Ann. Int. Med. **9**:115-122 (Aug.) 1935.

18. Camp, J. D., cited by Barnes.[4]

19. McGinn, S., and White, P. D.: Acute Cor Pulmonale, Resulting from Pulmonary Embolism: Its Clinical Recognition, J. A. M. A. **104**:1473-1480 (April 27) 1935.

20. Barnes, A. R.: Diagnostic Electrocardiographic Changes Observed Following Acute Pulmonary Embolism, Proc. Staff Meet., Mayo Clin. **11**:11-13 (Jan. 2) 1936.

In this small group, prompt diagnosis and preparation might have allowed emergency embolectomy in 6 cases.

Lord [21] found records of 59 fatal pulmonary embolisms in the Massachusetts General Hospital. In this group only 20 per cent of the patients died in ten to twenty minutes. He stated that complete occlusion of both primary pulmonary branches kills in one to two minutes. If the patient lives longer it is presumptive evidence that occlusion is incomplete. A patient may survive total obstruction of one main branch if the sudden strain on the circulation is not too great.

Fifteen of our 24 patients died suddenly. In this group occlusion of the main pulmonary artery and its large branches was observed in 4 instances, occlusion of the right and left branches together in 5, occlusion of the common artery and one large branch in 1 and occlusion of the common artery alone in 1 and of one large branch alone in 4.

TABLE 2.—*Sites of Occlusion and Periods of Survival*

Period of Survival	Arteries Occluded		
	Common	Right	Left
Few moments	+	+	+
8 minutes	0	+	+
30 minutes	0	+	+
35 minutes	0	0	+
60 minutes	0	+	+
90 minutes	0	+	0
2½ hours	+	+	+
3 hours	+	0	+
24 hours	0	+	+

The survival periods and sites of occlusion in our other 8 cases are given in table 2.

In the patient who survived twenty-four hours both right and left branches were involved. One patient with partial occlusion of the common artery and both large branches lived two and one-half hours.

One must not think of the mechanical plug in the pulmonary arteries as large enough to block the circulation. In fact, numerous scattered small emboli in the lungs can produce the same symptom complex, and the surgeon must not be chagrined if he attempts embolectomy and finds no large plugs. In the cases we have observed it has never seemed that the emboli were large enough to block the vessels and obliterate the lumen mechanically. There is evidently an additional element of profound reflex sympathetic inhibition causing a spasm of all the pulmonary circulation. Barnes [2] cited evidence in favor of the hypothesis that sympathetic inhibition plus humoral factors of alkalinity and acidity explain the attack of shock and the sudden death.

21. Acute Diverticulosis and Massive Pulmonary Embolism, Cabot Case 19052, New England J. Med. **208**:260-263 (Feb. 2) 1933.

Summarizing available data on our second point, the necessity of recognizing nonfatal as well as the premonitory signs of fatal pulmonary embolism, we may conclude:

1. In many instances (33 per cent in our series) nonfatal attacks of pulmonary embolism precede the fatal attack by hours to many days.

2. Signs of nonfatal embolism or the early signs of fatal embolism are not cyanosis and dyspnea, but are those of shock, with or without dyspnea.

3. Nonfatal emboli may be small, producing only pleuritic pain, fever and rapid pulse. They may be larger and may or may not produce infarction when they lodge in the lung substance, depending on the efficiency of the circulation in the lung. They may be massive but nonlethal, with the production of acute cor pulmonale and electrocardiographic signs differing from those of cardiac infarction.

4. Fatal pulmonary embolism in 30 to 60 per cent of cases causes death within a period of thirty minutes to twenty-four hours, allowing sufficient time for operative intervention in some cases if the diagnosis can be made and the emergency is anticipated.

POSSIBILITY OF PREVENTION AND TREATMENT

First in prevention must come the realization of the problem. One must recognize the greater risk for the obese female patient over 50, with a low or normal blood pressure. Aside from the added risk of sex and age, operations on the abdomen add to the risk. Trauma with much tissue mutilation may be complicated by thrombosis and embolism. Childbirth, acute febrile disturbances (such as pneumonia or typhoid fever) and cardiac decompensations of all kinds, but especially those with auricular fibrillations, as well as all types of phlebitis, may be complicated by embolism.

Next, efforts should be made to prevent thrombosis and embolism. These are in use in some clinics. Robertson [6] on the basis of a large postmortem experience advocated in postoperative cases massage, passive and active motions of the legs, frequent moving and turning of the body and deep breathing to facilitate the circulation of blood in the dependent portions, local use of heat or of vascular stimulants, such as thyroid, used conservatively.

Walters [22] in 1930 reported the results of four and a half years' experience in attempting to reduce the incidence of postoperative embolism by giving thyroid to 4,500 patients. The incidence was only

22. Walters, W.: A Method of Reducing the Incidence of Fatal Postoperative Pulmonary Embolism: Results of Its Use in Four Thousand and Five Hundred Surgical Cases, Surg., Gynec. & Obst. **50**:154-157 (Jan.) 1930.

0.09 per cent, as compared with 0.34 per cent in series in which thyroid was not given.

Barnes [2] stated that Willius has employed since 1926 at the Mayo Clinic centripetal massage of the legs of patients hospitalized for cardiac disease, and no deaths from massive embolism have occurred in the cardiac disease service during this period. In Gray's surgical service in the same institution a postoperative program places the patient in the Trendelenburg position for twenty-four hours after operation; carbon dioxide by inhalation is given several times day and night for the first forty-eight hours; frequent deep breathing is urged; early coughing is encouraged; the legs are kept warm on the operating table and afterward, and frequent massage of the legs practiced during the first forty-eight hours and twice daily until the patient is out of bed. With this program there have been no deaths from embolism in 750 consecutive operations, mostly laparotomies.

In view of the demonstrated effect of proteins on the tendency of platelets to agglutinate, it would seem advisable to keep the protein intake low for two weeks after operation.

Since tissue juices increase coagulability of the blood and later provoke increased platelet counts, every effort should be made to keep damage to tissues at a minimum.

Dehydration with increased viscosity of the blood favors clotting, and closer attention to fluid intake and output can be expected to cut the incidence of thrombosis.

For a patient who has had a mild nonfatal attack special care must be used to avoid a subsequent fatal attack. Greater care must be used in curtailing his efforts. He must not be allowed out of bed as soon as usual, and preparations should be made for subsequent attacks. A syringe containing ½ grain (0.032 Gm.) of papaverine hydrochloride for intravenous use should be kept at hand, as this drug tends to relieve the spasm of the pulmonary vessels. A sterile surgical set should be kept at hand if a Trendelenburg operation is to be attempted. An oxygen tent should be available.

SUMMARY AND CONCLUSIONS

Twenty-four instances of fatal pulmonary embolism in 1,781 autopsies are recorded.

The following factors favor embolism: age between 40 and 60, female sex, operations on the abdomen and the pelvis, cardiac disease and obesity with normal or subnormal blood pressure.

In our 24 cases 8 patients had nonfatal embolism preceding the fatal attack by three hours to thirty days. Such nonfatal embolism occurred on an average of five days after operation or trauma.

Shock should be the criterion for diagnosing embolism. The most common symptoms in our series were perspiration, imperceptible pulse, weakness and pain in the chest.

In our series the average postoperative fatal embolism occurred on the sixteenth day, while the death from post-traumatic embolism occurred on the forty-first day.

Fifteen patients in our series died suddenly. In this group autopsy disclosed occlusion of the main pulmonary artery and its main branches in 4 instances and occlusion of both large branches in 5.

The remaining 9 patients lived from eight minutes to twenty-four hours, allowing sufficient time for emergency embolectomy in 5 cases if conditions had been favorable.

ECTOPIC PREGNANCY, A DIAGNOSTIC PROBLEM IN GYNECOLOGY

REPORT OF A CASE

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The case here described is of interest and importance because it represents a limited group of tubal gestations in which tests for pregnancy yield negative reactions. It brings to attention, also, a limitation of the pregnancy test infrequently set forth in the literature.

An intricate diagnostic problem arose in connection with a patient with a suspected tubal abortion. The classic clinical evidence was not present. Two tests for pregnancy gave negative results, and since curettings revealed no decidual reaction, laparotomy was delayed for thirty-five days. The reason for the inadequacy of the test in this instance is clearly illustrated by the pathologic findings. Consideration of this factor is therefore of utmost value in the diagnosis of tubal abortion.

REPORT OF CASE

S. B., aged 28, had been married six years and had always had normal and regular menstrual periods. The past history was irrelevant except for an induced abortion in 1931. For four years she had been unable to become pregnant. Normal in every respect, the last menstrual period (on Dec. 8, 1937) was followed by continuous but moderate staining, and two weeks later (on December 21), when the patient was first examined, bleeding was still present.

Somatically, physical findings were within normal limits. With the exception of a walnut-sized, nontender mass in the left adnexal region, not unlike a cystic ovary, and a uterus of normal size, drawn slightly to the left, the pelvic examination revealed nothing significant.

The patient was referred to the Mount Sinai Hospital for observation, with a tentative diagnosis of ectopic pregnancy. In spite of a negative result of the Friedman test (with 2 rabbits) diagnostic curettage was performed, but in view of the absence of decidual reaction in the endometrium (fig. 1), presumptive evidence of pregnancy, and the cessation of staining, the patient was discharged from the hospital.

Ten days later, on Jan. 5, 1938, there was a normal menstrual period, which again ushered in constant uterine staining. Endocrine or blood dyscrasia, endometriosis and follicle cyst of the ovary, as well as inflammation, were then considered as causes; but the basal metabolism, the blood count, the sedimentation rate, the clotting and coagulation time, the results of urinalysis and the temperature were all within normal range. After eighteen days of staining the patient

From the Gynecologic Service of the Mount Sinai Hospital.

noticed a sharp, constant ache in the left lower quadrant of the abdomen, radiating to the left lumbar region. She also voided urine frequently. The bleeding continued unchanged. At this time the mass was slightly larger but still was not tender. In view of its increasing size, laparotomy was considered imperative.

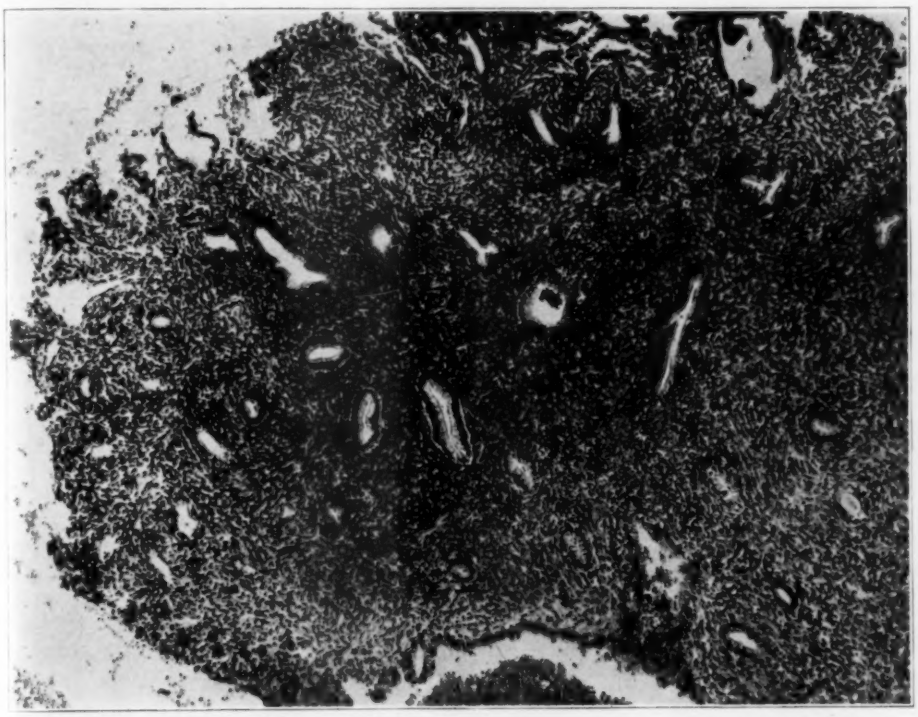

Fig. 1.—Endometrium in the resting stage found on curettage one week before the menses. No decidual reaction was noted. Secretory endometrium was also absent.

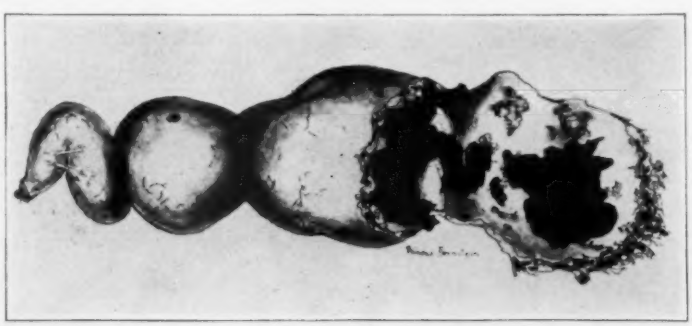

Fig. 2.—Left tube, showing the ruptured, fimbriated end and a blood clot containing villi. Note the kinking at the proximal end caused by adhesions.

The patient was again hospitalized, and at operation, on January 28, an ectopic mole was removed. The result of the Friedman test with urine catheterized preoperatively was again negative.

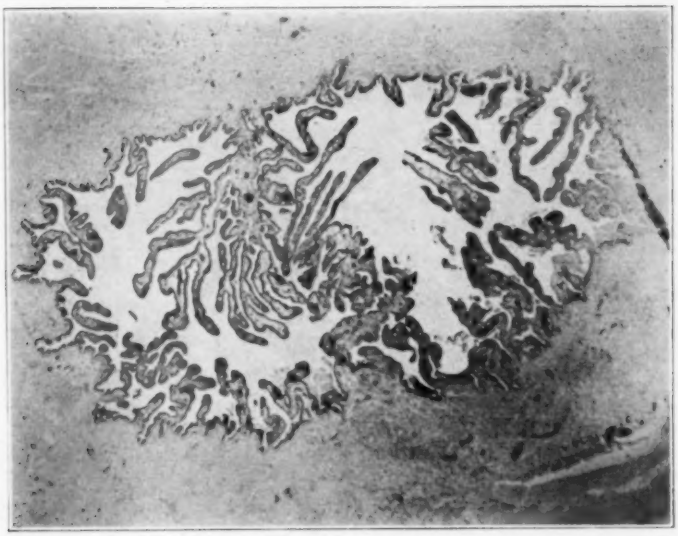

Fig. 3.—Low power photomicrograph of the cross section of the proximal end of the fallopian tube, showing chronic inflammation.

Fig. 4.—High power photomicrograph of a section of the blood clot, showing several chorionic villi.

Examination of the operative specimen revealed an enlarged left tube kinked by adhesions at the proximal end (fig. 2). Beyond the distended, gaping fimbriated portion on a bed of adhesions connecting it to the sigmoid flexure of the colon, lay a free and detached blood clot 1½ inches (3.7 cm.) in diameter; this contained the pregnancy mole, which had been completely blown out through the ruptured ampulla. There was 60 cc. of free blood in the pelvis. The left ovary, enlarged to the size of a large plum by two follicle cysts, was prolapsed.

Microscopic examination of the serial sections of the fallopian tube showed no chorionic remnants or decidual reaction (fig. 3). There was evidence of low grade inflammation. The only villi (fig. 4) observed were in the blood clot previously described. It was therefore concluded that the gestation had separated entirely from its mural attachment.

A positive result of the Friedman test is usually authentic if two test animals are used. On the other hand, the frequent false negative reactions obtained in the presence of a proved viable embryo are ascribed either to an insufficient quantity of the gonadotropic principle in the specimen of urine or to the test animals' insensitivity to that principle.

However, complete cessation of the gonadotropic response is effected also by detachment of the gestational mole from its tubal site of nidation. The pregnancy stimulus is in this manner separated from the maternal circulation. Thus the cause of the misleading negative results of the Friedman tests is made clear.

The presence of a decidual reaction in the endometrium is suggestive and significant but not pathognomonic of ectopic gestation. It is not, furthermore, a constant finding. The absence of this reaction, therefore, did not exclude the possibility of tubal pregnancy.

SUMMARY

A case of ectopic pregnancy is described.

The report is warranted because of the marked clinical atypism and because it represents a small but important group of tubal pregnancies in which the Friedman test gives negative results. The diagnostic error is therefore high. About 20 per cent of women with ectopic pregnancy are reported as giving negative reactions to this test.

The principal unusual features are: (*a*) two normal menses during a two month period of staining, (*b*) negative reactions to two Friedman tests performed within a fortnight's interval, and (*c*) curettings obtained one week before the menses, during the episode of staining, containing resting or proliferative endometrium. Decidual reaction was not observed.

A growing, nontender mass, continuous staining and a short episode of pain finally warranted laparotomy in spite of the clinical and laboratory atypism. These were the only positive findings.

The inadequacy of the Friedman phenomenon in this type of tubal abortion is due to the complete detachment of the gestation mole from the tubal wall, effecting a cessation in production of the gonadotropic hormone and its consequent absence in the patient's urine. The tests therefore gave negative results.

This limitation of the phenomenon must always be borne in mind when a diagnosis of ectopic pregnancy is considered.

The proliferative or resting endometrium (normally present in the preovulatory phase of the menstrual interval) found in this patient one week before the menses is difficult to explain.

INTESTINAL OBSTRUCTION IN MAN

ALTERATIONS IN THE SERUM BASES AND THEIR SIGNIFICANCE

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AND

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ROCHESTER, MINN.

For more than twenty-five years the alterations which take place in the chemistry of the blood during intestinal obstruction have interested many workers, who have sought to explain the course and termination of unrelieved obstruction on the basis of the changes observed in the chemical constituents of the blood. In their turn, dehydration,[1] azotemia[2] and hypochloremia following excessive loss of chloride by vomiting[3] have all been incriminated, but not one of these factors suffices to explain completely the clinical progress of patients who have intestinal obstruction. Falconer and Lyall[4] observed the changes in the constituents of the blood in a number of cases of intestinal obstruction and found that uniformity does not characterize the biochemical changes in the blood of patients who have obstruction at any particular level of the intestine. In their cases, increase in the concentration of urea in the blood was the most constant change encountered, but observations on the individual bases of the serum were not made.

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The work presented in this paper was done on special assignment in the Mayo Foundation from the University of Otago, New Zealand.

From the Section on Clinical Biochemistry (Drs. Falconer and Osterberg) and the Division of Medicine (Dr. Bargen), the Mayo Clinic.

1. Hartwell, J. A., and Hoguet, J. P.: Experimental Intestinal Obstruction in Dogs with Especial Reference to the Cause of Death and the Treatment by Large Amounts of Normal Saline Solution, J. A. M. A. **59**:82-87 (July 13) 1912.

2. Cooke, J. V.; Rodenbaugh, F. H., and Whipple, G. H.: Intestinal Obstruction: VI. A Study of the Non-Coagulable Nitrogen of the Blood, J. Exper. Med. **23**:717-738 (June) 1916.

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In 1937, Scudder, Zwemer and Truszkowski [5] reported that experimental obstruction of the alimentary tract at any level in cats was followed by elevation of the concentration of potassium in the blood to such heights as to suggest that hyperpotassemia was the cause of death. Their observations were based on determinations made on whole blood. This procedure is permissible with the cat, because in this animal the potassium content of the cells and of the plasma is similar, and the concentration in each rises and falls together. These workers ascribed the rise in the potassium concentration in the blood to the liberation of potassium from the tissues as the result of dehydration and the action of bacterial toxin, and they remarked on the similarity between the alterations they observed and those associated with Addison's disease. In a later paper [6] they showed that a similar rise in the concentration of potassium in the blood occurred in cats that had complete intestinal fistulas; in addition, Cutler and Pijoan [7] found that hyperpotassemia occurred also in dogs the intestines of which had been experimentally obstructed and that the intravenous injection of solutions of potassium chloride precipitated death.

Apart from isolated observations,[8] little notice had been taken of the changes which occur in the calcium content of the blood until Ruggieri [9] in 1935 reported that the level tended to rise after experimental obstruction and that this rise was greater the higher the level at which obstruction was present in the bowel. An explanation of the mechanism concerned was not forthcoming. As regards the other bases of the blood, particular attention has been paid in the past to alterations in the sodium content, and it has been clearly shown [10] that the concen-

5. Scudder, J.; Zwemer, R. L., and Truszkowski, R.: Potassium in Acute Intestinal Obstruction, Surgery **1**:74-91 (Jan.) 1937.

6. Scudder, J., and Zwemer, R. L.: The Effect of Complete Intestinal Fistula on Blood Potassium, Surgery **2**:519-531 (Oct.) 1937.

7. Cutler, E. C., and Pijoan, M.: Certain Chemical Factors in Experimental High Intestinal Obstruction, Surg., Gynec. & Obst. **64**:892-894 (May) 1937.

8. Hastings, A. B.; Murray, C. D., and Murray, H. A., Jr.: Certain Chemical Changes in the Blood After Pyloric Obstruction in Dogs, J. Biol. Chem. **46**:223-232 (March) 1921.

9. Ruggieri, E.: Calcemia ed occlusione intestinale, Policlinico (sez. chir.) **42**:669-684 (Nov.) 1935.

10. (*a*) Ruggieri.[9] (*b*) Gamble, J. L., and Ross, S. G.: The Factors in the Dehydration Following Pyloric Obstruction, J. Clin. Investigation **1**:403-423 (June) 1925. (*c*) Gamble, J. L., and McIver, M. A.: A Study of the Effects of Pyloric Obstruction in Rabbits, ibid. **1**:531-545 (Aug.) 1925. (*d*) Atchley, D. W., and Benedict, E. M.: The Distribution of Electrolytes in Intestinal Obstruction, J. Biol. Chem. **75**:697-702 (Dec.) 1927. (*e*) Haden, R. L., and Orr, T. G.: The Sodium Content of the Blood of the Dog After Experimental Intestinal Obstruction, J. Exper. Med. **41**:119-127 (Jan.) 1925.

tration of this base in the plasma tends to decrease, but not to the same extent as that of plasma chloride. The total content of base in the plasma also tends to fall.[11]

These reports, particularly those dealing with the serum potassium, prompted us to ascertain whether similar variations in the serum bases occurred in clinical obstruction in man. During a period of six months, therefore, we investigated the alterations in the chemical constituents of the blood of patients who had intestinal obstruction. Our method was to collect samples of blood both during obstruction and at frequent intervals subsequently, and thereby we were able to observe not only the biochemical changes present during obstruction but the alterations which took place as the patient proceeded toward recovery or death. The findings in individual cases appear in table 1.

To obtain our quantitative data, we employed the following technical procedures: for the determination of the urea content of whole blood, the Van Slyke and Cullen modification of the Marshall aeration and titration method;[12] for chloride in plasma, the Osterberg and Schmidt method;[13] for the carbon dioxide–combining power of the plasma, the method of Van Slyke and Stadie;[14] for the sodium content of the serum, the method of Kramer and Gittleman;[15] for the potassium content of the serum, the method of Kramer and Tisdall;[16] for the calcium content of the serum, the method of Clark and Collip;[17] and for the total base content of the serum, the method of Stadie and Ross.[18]

COMMENT

These reports of cases show that during acute intestinal obstruction, both mechanical and paralytic, in man, the concentration of serum

11. Gamble and Ross.[10b] Gamble and McIver.[10c] Atchley and Benedict.[10d]

12. Van Slyke, D. D., and Cullen, G. E.: A Permanent Preparation of Urease, and Its Use in the Determination of Urea, J. Biol. Chem. **19**:211-228, 1914.

13. Osterberg, A. E., and Schmidt, E. V.: The Estimation of Plasma Chlorides, J. Lab. & Clin. Med. **13**:172-175 (Nov.) 1927.

14. Van Slyke, D. D., and Stadie, W. C.: The Determination of the Gases of the Blood, J. Biol. Chem. **49**:1-42 (Nov.) 1921.

15. Kramer, B., and Gittleman, I.: An Iodometric Method for the Determination of Sodium in Small Amounts of Serum, J. Biol. Chem. **62**:353-360 (Dec.) 1924.

16. Kramer, B., and Tisdall, F. F.: A Clinical Method for the Quantitative Determination of Potassium in Small Amounts of Serum, J. Biol. Chem. **46**:339-349 (April) 1921.

17. Clark, E. P., and Collip, J. B.: A Study of the Tisdall Method for the Determination of Blood Serum Calcium with a Suggested Modification, J. Biol. Chem. **63**:461-464 (March) 1925.

18. Stadie, W. C., and Ross, E. C.: A Micro Method for the Determination of Base in Blood and Serum and Other Biological Materials, J. Biol. Chem. **65**: 735-754 (Oct.) 1925.

TABLE 1.—*Summary of Cases*

Case	Clinical Data	Chemical Examination of the Blood							Comment
		Date	Blood Urea, Mg. per 100 Cc.	Plasma NaCl, Mg. per 100 Cc.	Plasma CO_2-Combining Power, Vol. per 100 Cc.	Serum K, Mg. per 100 Cc.	Serum Na, Mg. per 100 Cc.	Serum Ca, Mg. per 100 Cc.	Hematocrit, per Cent	
1	Man aged 35; pyloric obstruction complicated by uremic intoxication; improved under medical management before operation was performed	12/29/37	58	437	105.2	....	...	....	..	On admission; retention regimen with intravenous fluids
		12/30/37	48	468	98.2	11.5	319	....	38	2,000 cc. 0.9% NaCl daily
		1/ 3/38	16	611	82.4	14.1	319	....	..	1,000 cc. 5% dextrose daily
		1/ 6/38	16	582	79.6	16.3	336	....	40	
		1/ 8/38	Operation performed							Posterior gastroenterostomy
		1/17/38	14	508	61.3	16.0	336	....	39	Before discharge
2	Man aged 39; pyloric obstruction complicated by uremic intoxication; improved under medical management before operation was performed	12/ 3/37	60	472	93.1	12.5	...	....	46	On admission; retention regimen with intravenous fluids
		12/ 4/37	58	455	93.9	....	...	....	44	2,000 cc. 0.9% NaCl daily
		12/ 6/37	38	574	69.2	14.8				
		12/ 7/37	24	623	72.1	15.1	308	....	36	1,000 cc. 5% dextrose solution
		12/ 8/37	28	594	60.7	16.2	...	....	35	Before operation
		12/ 8/37	Operation performed							Posterior gastroenterostomy
		12/16/37	24	624	64.5	21.7	...	....	37	On recovery
3	Man aged 36; uremic intoxication complicating pyloric stenosis, with vomiting secondary to a penetrating duodenal ulcer; responded to medical management prior to operation	3/ 2/38	66	578	74.9	17.6	319	....	40	On admission; retention regimen and intravenous saline and dextrose solutions daily
		3/ 4/38	34	561	64.5					
		3/ 9/38	30	511	76.6	16.8	319	12.2	42	Improvement
		3/ 9/38	Operation performed							Partial gastrectomy
		3/21/38	27	578	57.3	16.0	308	9.6	33	On recovery
4	Man aged 59; uremic intoxication and debility complicating carcinomatous obstruction of pyloric antrum; improved with retention regimen and intravenous saline solution; operation followed by recovery	3/ 5/38	46	578	60.7	23.0	313	....	36	On admission; retention regimen and intravenous saline solutions
		3/ 7/38	38	676	66.4					
		3/ 9/38	22	627	58.9	19.4	319	9.5	35	Improvement
		3/ 9/38	Operation performed							Partial gastrectomy
		3/21/38	30	594	66.4	17.5	313	7.9	30	On recovery
		4/ 1/38	16	578	65.5	18.6	302	8.8	40	11 days later
5	Man aged 53; mild degree of alkalosis complicating pyloric stenosis with vomiting; relief followed medical management prior to operation	2/ 8/38	42	561	73.0	18.0	331	9.2	34	Retention regimen with 2,000 cc. Ringer's solution intravenously daily
		2/10/38	30	569	72.1					
		2/11/38	26	594	69.2	16.8	317	9.0	32	
		2/11/38	Operation performed							Posterior gastroenterostomy
		2/22/38	32	602	57.9	18.6	308	8.4	31	On recovery
6	Man aged 37; mild degree of alkalosis	12/14/37	32	527	79.6	13.6	319			

6	Man aged 37; mild degree of alkalosis complicating pyloric stenosis with vomiting; responded to medical management prior to operation	12/14/37	32	587	70.2	13.6	319	....	40	Retention regimen; intravenous saline solutions daily
		12/16/37	24	639	64.6	15.2	302	....	42	250 cc. blood transfusion
		12/17/37	Operation performed							Posterior gastroenterostomy
		1/21/38	16	578	64.9	24.4	319	....	42	On recovery
7	Man aged 48; mild degree of alkalosis complicating pyloric stenosis with vomiting; responded to medical management prior to performance of operation	2/16/38	26	544	70.2	26.0	308	9.2	23	Retention regimen; intravenous saline solutions daily
		2/19/38	18	619	57.9					
		2/21/38	18	592	58.9	26.4	302	9.2	20	600 cc. blood transfusion
		2/24/38	16	602	61.7	24.6	308	9.6	27	
		2/24/38	Operation performed							Posterior gastroenterostomy
		2/28/38	12	571	57.1	23.6	302	9.0	24	Fourth day after operation
		3/ 8/38	20	561	58.9	23.8	302	10.0	26	On recovery
8	Man aged 57; acute obstruction of gastrojejunostomy stoma which commenced 4 days prior to admission; treated conservatively (retention regimen, intravenous fluids, gastric aspirations) with definite improvement in patient's general condition but severe gastric retention (as much as 2,400 cc. daily) persisted and was relieved only by operation	4/ 3/38	100	384	98.0	....	...	....	..	On admission; intravenous Ringer's and dextrose solutions daily
		4/ 4/38	60	489	93.9	19.8	308	9.4		
		4/ 6/38	82	525	69.2	18.7	308	9.2	43	General condition improving but severe degree of gastric retention persisting
		4/ 9/38	40	585	74.0	14.5	319	9.3	42	
		4/13/38	28	551	75.8	14.8	290	8.9	40	
		4/15/38	22	574	68.3					
		4/15/38	Operation performed							Reduction of acute angulation of efferent jejunal loop
		4/22/38	16	532	67.3	15.0	...	7.7	34	
		4/27/38	20	559	60.7	14.9	319	8.7	33	Uneventful convalescence; discharged from hospital
9	Boy aged 3 years; signs of acute intestinal obstruction developed while in hospital; operation disclosed internal herniation of the jejunum through mesenteric hiatus; improvement followed surgical relief, but edema of the extremities developed postoperatively; this disappeared when saline therapy was discontinued	12/30/37	46	...	55.1	....	...	....	..	On admission; no obstruction
		1/ 1/38	159	489	65.5	....	...	....	..	Signs of obstruction developed; intravenous saline solutions commenced
		1/ 2/38	81	644	....	....	...	....	..	Immediately before operation
		1/ 2/38	Operation performed							
		1/ 3/38	90	710	....	12.1	342	....	41	12 hours after operation
		1/ 4/38	46							
		1/ 6/38	30	627	....	11.0	358	....	..	Obstruction relieved; edema present; salines discontinued
		1/13/38	22	594	62.6	22.0	322	....	..	On recovery
10	Man aged 65; obstructed ventral hernia involving midileum; acute symptoms for two days; responded to conservative management (duodenal suction and intravenous fluids) prior to operation	2/11/38	42	611	42.8	17.9	319	8.9	39	On admission; intravenous saline and dextrose solutions daily
		2/14/38	30	611	57.0	19.3	319	8.8	34	Definite improvement
		2/14/38	Operation performed							Operative repair of hernia
		2/28/38	26	561	73.0	16.3	302	8.1	32	On recovery
11	Woman aged 54; obstructed incisional hernia involving small bowel (roentgenologic diagnosis); responded to conservative treatment	3/ 9/38	28	627	....	18.5	325	8.8	..	On admission; occasional vomiting; symptoms mild
		3/11/38	20	627	60.7	17.5	308	10.2	44	
		3/22/38	28	602	58.9	17.5	308	9.9	40	On recovery

TABLE 1.—*Summary of Cases—Continued*

Case	Clinical Data	Date	Chemical Examination of the Blood: Blood Urea, Mg. per 100 Cc.	Plasma NaCl, Mg. per 100 Cc.	Plasma CO_2-Combining Power, Vol. per 100 Cc.	Serum K, Mg. per 100 Cc.	Serum Na, Mg. per 100 Cc.	Serum Ca, Mg. per 100 Cc.	Hematocrit, per Cent	Comment
12	Woman aged 79; acute obstruction of ileum (roentgenologic diagnosis); duration one or two days; responded to conservative management with intravenous saline solutions and duodenal suction; although concentration of serum potassium was not determined during period of obstruction, note rise on recovery	3/23/38	96	503	....	....	...	....	..	During obstruction; saline solutions given prior to analysis of blood
		3/28/38	26	600	58.9	10.2	313	7.5	35	Obstruction relieved; no further saline solutions given
		4/ 1/38	28	561	65.5	15.8	312	8.4	39	On recovery
13	Woman aged 86; acute obstruction of terminal ileum attributable to intraperitoneal adhesions (roentgenologic diagnosis); treated conservatively with duodenal suction, intravenous fluids; death ensued	12/ 8/37	44	569	53.2	20.4	...	....	40	On admission; nasal suction and intravenous saline solutions
		12/ 9/37	78	563	37.2	15.9	...	8.3	41	Before death
14	Woman aged 47; acute obstruction of transverse colon attributable to intra-abdominal adhesions (roentgenologic diagnosis); treated conservatively by means of duodenal suction and intravenous saline solutions; recovery ensued	12/ 4/37	50	470	80.6	14.5	...	....	34	Before treatment was instituted; 2,000 cc. 0.9% NaCl daily
		12/ 6/37	46	549	63.6	14.5	...	9.5	33	Intravenous fluids discontinued
		12/ 8/37	24	577	60.7	15.1	...	....	34	On recovery
		12/22/37	18	550	67.3	17.8	...	....	37	
15	Woman aged 64; carcinoma of rectum obstructing lumen; treated conservatively by means of intravenous saline solutions, stupes to abdomen and rectal irrigations; relief of obstructive symptoms ensued	1/ 3/38	48	611	50.4	17.2	325	8.7	46	On admission; conservative treatment with intravenous saline solutions, stupes and rectal irrigations
		1/ 3/38	42	651	56.0	19.0	...	9.3	..	
		1/ 6/38	26	635	60.7					
		1/ 7/38	16	594	63.4	19.3	342	9.8	45	Symptoms relieved
16	Woman aged 42; acute-on-chronic obstruction from carcinoma of the rectum of 4 days' duration; management conservative; complete relief followed performance of operation	12/15/37	32	619	64.5	18.5	...	....	30	On admission; prepared for operation
		12/19/37	Operation performed.....							Colostomy
		1/12/38	18	578	65.5	22.9	313	....	36	On recovery
17	Woman aged 57; acute-on-chronic obstruction from carcinoma of sigmoid colon; failed to respond to conservative measures; at operation, colonic distention grade 3 was found; recovery ensued	11/23/37	24	594	65.5	14.7	...	....	41	On admission; dextrose and saline solutions intravenously
		11/24/37	24	611	59.8	14.2	...	9.3	38	Before operation
		11/24/37	Operation performed.....							Laparotomy; colostomy
		12/ 9/37	18	563	57.9	19.5	...	....	37	On recovery

18	Woman aged 43; thrombosis of the superior mesenteric vessels following operation for partial and intermittent jejunal obstruction	3/ 3/38	24	635	57.9	19.0	302	....	..	On admission; occasional vomiting only
		3/ 5/38	Operation performed							Resection of several coils of jejunum
		3/ 8/38	64	710	58.9	15.8	350	8.9	36	Third day after operation; saline solutions given intravenously
		3/ 9/38	70	775	50.4	15.3	354	8.7	34	Died 24 hours later
19	Man aged 65; postoperative distention following left inguinal colostomy; relieved by conservative measures (duodenal suction, intravenous saline solutions, hot abdominal packs); recovery occurred	11/17/37	40	660	50.4	15.9	...	....	41	Second day after operation; treatment begun
		12/13/37	32	594	54.3	18.2	...	....	42	On recovery
20	Woman aged 59; moderate degree of postoperative distention following colostomy for carcinoma recti; colostomy loop opened on second day; treated conservatively, with recovery	2/ 3/38	14	683	59.8	14.2	345	9.7	32	Third day after operation; receiving saline solutions intravenously
		2/14/38	20	578	66.4	14.6	308	9.3	32	Seven days after clinical recovery
		2/21/38	14	590	64.5	20.6	319	10.0	34	Fourteen days after clinical recovery
21	Woman aged 42; general peritonitis with paralytic ileus following right hemicolectomy performed for carcinoma of ascending colon; death occurred five days after operation; the single serum potassium reading was obtained during a period of extreme distention	11/24/37	64	660	57.9	20.3	...	....	40	Fourth day after operation; receiving solutions of dextrose and saline solutions intravenously
		11/25/37	94	619	57.7	....	...	....	..	Died a few hours later
22	Man aged 48; generalized peritonitis with paralytic ileus following laparotomy which revealed inoperable carcinoma of colon; died three days after operation	2/18/38	72	585	44.7	23.1	302	9.8	51	Condition of the blood a few hours before death
23	Woman aged 70; paralytic ileus from peritonitis following anterior resection of sigmoid colon; treated conservatively with duodenal suction, intravenous saline solutions, hot abdominal packs; death ensued	11/30/37	42	678	59.8	....	...	....	40	Fourth day after operation
		12/ 1/37	54	658	62.6	15.6	...	11.0	41	Condition deteriorating; died 12 hours later
24	Woman aged 56; paralytic ileus following sigmoid colostomy performed 12/14/37; treated conservatively with duodenal suction, intravenous fluids and hot abdominal packs; death ensued; at necropsy, generalized peritonitis was observed	12/17/37	34	620	48.5	17.2	...	....	38	Third day after operation; gross abdominal distention
		12/18/37	42	583	57.0	21.6	...	....	40	
		12/20/37	24	591	61.4	16.8	...	....	36	Improved
		12/22/37	36	544	61.7	16.5	...	....	37	Relapse; severe degree of distention
		12/24/37	18	602	73.9	....	...	....	..	Improved
		12/27/37	16	676	76.2	16.5	...	....	41	Condition deteriorating
		12/29/37	14	497	78.2	16.2	313	....	..	Died 24 hours later

TABLE 1.—*Summary of Cases—Continued*

Case	Clinical Data	Date	Chemical Examination of the Blood: Blood Urea, Mg. per 100 Cc.	Plasma NaCl, Mg. per 100 Cc.	Plasma CO_2-Combining Power, Vol. per 100 Cc.	Serum K, Mg. per 100 Cc.	Serum Na, Mg. per 100 Cc.	Serum Ca, Mg. per 100 Cc.	Hematocrit, per Cent	Comment
25	Woman aged 58; acute obstruction of colon following ingestion of barium sulfate meal in presence of carcinoma of sigmoid colon; obstruction relieved by conservative means; colostomy then performed preliminary to later radical excision of growth; patient showed a severe degree of listlessness which improved after the addition of potassium and calcium salts to the intravenous solutions	1/ 9/38	34	594	54.0	....	328	10.2	..	On admission; intravenous dextrose and saline solutions daily
		1/11/38	16	...	....	20.0	322	....	36	
		1/13/38	14	...	....	11.8	319	8.8	36	Obstruction relieved but listlessness present
		1/15/38	14	585	68.3	11.9	322			
		1/15/38	Operation performed							
		1/18/38	14	611	65.5	14.3	316	8.6	35	Third day after operation
			Received 2 Gm. KCl and 1 Gm. $CaCl_2$							
		1/19/38	14	563	73.0	14.5	325	8.8	36	Intravenous dextrose solutions daily
			Received 4 Gm. KCl and 2 Gm. $CaCl_2$							
		1/21/38	24	569	71.1	14.9	325	9.2	41	General condition improving
		1/24/38	26	575	66.4	17.3	324	9.8	40	
			Received 4 Gm. KCl and 2 Gm. $CaCl_2$							
		1/26/38	22	569	65.5	22.0	313	9.7	41	Definite improvement; intravenous fluids stopped
		1/31/38	32	619	58.9	20.3	308	9.8	38	On recovery
26	Woman aged 69; paralytic ileus following exteriorization of sigmoid colon for diverticulitis; treated conservatively (duodenal suction, intravenous fluids) with restoration of function of bowel on the 11th day; definite languor persisted and was not relieved until potassium and calcium salts were added to the intravenous fluids following the fifteenth day	12/17/37	44	710	60.7	16.0	...	....	36	Fourth day after operation; intravenous dextrose and saline solutions daily
		12/18/37	48	627	57.0	11.1	...	....	36	
		12/19/37	51	669	54.1	10.7	...	....	38	
		12/21/37	40	683	51.3	9.5	...	....	40	
		12/24/37	24	647	63.3	12.8	336	....	39	Bowels functioning well but severe languor present
		12/26/37	18	567	73.0	11.6	342	7.7	39	Intravenous dextrose solutions daily
		12/29/37	24	483	80.6	8.7	325	8.7	39	
			Received 1 Gm. KCl and 1 Gm. $CaCl_2$							
		12/30/37	24	479	83.4	9.9	328	9.0	42	Intravenous NaCl solutions restored
			Received 2 Gm. KCl and 1 Gm. $CaCl_2$							
		12/31/37	24	541	82.4	10.1	328	8.8	39	
			Received 2 Gm. KCl and 1 Gm. $CaCl_2$							
		1/ 2/38	18	583	58.0	12.1	342	8.5	37	Definite improvement; intravenous solutions discontinued
		1/ 5/38	26	594	79.6					
		1/ 7/38	26	594	69.2	17.2	325	9.2	39	
		1/10/38	26	587	59.0	16.4	323	9.4	38	On recovery
27	Man aged 70; paralytic ileus following temporary ileostomy performed for subacute obstruction secondary to carcinoma of the cecum; treated conservatively (duodenal suction, intravenous fluids, etc.) with eventual recovery; definite improvement followed the addition of potassium and calcium salts to the intravenous solutions	1/29/38	40	627	56.0	16.3	336	7.8	..	First day after operation; intravenous dextrose
		1/31/38	16	660	58.9	13.9	313	7.5	32	Saline and dextrose solutions daily
		2/ 2/38	20	619	....	....	...	....	..	500 cc. blood transfusion
			Received 1 Gm. $CaCl_2$							
		2/ 4/38	24	611	57.0	11.2	313	8.0	38	Dextrose solutions only
			Received 2 Gm. KCl and 1 Gm. $CaCl_2$							
		2/ 5/38	26	563	65.5	12.5	308	7.7	..	Definite general improvement; duodenal suction discontinued
			Received 3 Gm. KCl and 3 Gm. $CaCl_2$							
		2/ 7/38	16	553	62.5	11.1	290	8.0	..	NaCl and dextrose solutions restored
			Received 2 Gm. KCl and 2 Gm. $CaCl_2$							
		2/ 9/38	18	578	65.5	13.6	313	8.2	35	500 cc. blood transfusion
			Received 3 Gm. KCl and 2 Gm. $CaCl_2$							
		2/12/38	..	594	57.9	18.7	302	8.8	40	
		2/14/38	18	594	64.4	15.9	296	8.8	40	
			Received 4 Gm. KCl and 1 Gm. $CaCl_2$							
		2/16/38	22	594	55.1	18.3	293	8.4	37	Left hospital

potassium, instead of rising as it does in animals, tends to fall, often to a considerable degree. The concentrations of sodium and calcium in the serum tend to fall also, but their reduction is less severe than is that of potassium.

According to most authorities,[19] the potassium content of the serum in health ranges between 18 and 22 mg. per hundred cubic centimeters, but values outside these limits occasionally are found in healthy persons. Because of this wide range, the decision of whether or not the concentration of serum potassium in individual cases is altered should rest on changes found on repeated estimations rather than on single observations. The highest value that we observed for potassium was 26 mg. per hundred cubic centimeters of serum (case 7), a level which was maintained on recovery. On the other hand, the lowest value encountered was 9.5 mg. per hundred cubic centimeters (case 26). In 16 cases values less than 16 mg. per hundred cubic centimeters of serum were encountered (cases 1, 2, 6, 8, 9, 12, 13, 14, 17, 18, 19, 20, 23, 25, 26 and 27).

Since we began this investigation, Scudder, Zwemer and Whipple[20] have published their observations on 25 clinical cases of intestinal obstruction. Taking as the normal value for potassium 18 to 21 mg. per hundred cubic centimeters of plasma, they found that of 20 cases in which the blood was examined before saline therapy was begun, the potassium content of the plasma was elevated in 7 cases and decreased in 5. The highest reading recorded was 33.4 mg., and the lowest 13.4 mg., per hundred cubic centimeters. It is interesting to note that higher values than these have been found in the presence of other conditions. Keith and Binger[21] noted that 3 normal persons had concentrations of potassium of 33, 37 and 40 mg. per hundred cubic centimeters of serum respectively after the ingestion of potassium salts, without ill effects.

Our findings in clinical cases of intestinal obstruction are at variance with the published observations in cases of experimental obstruction in cats and dogs. However, we, too, have observed increase in the concentration of serum potassium in 3 dogs (table 2) in which the upper-

19. Whelan, M.: The Effect of Intravenous Injection of Inorganic Chlorides on the Composition of Blood and Urine, J. Biol. Chem. **63**:585-620 (April) 1925. Hoffman, W. S., and Jacobs, H. R. D.: The Partition of Potassium Between the Serum and Corpuscles in Health and Disease, J. Lab. & Clin. Med. **19**:633-644 (March) 1934. Kramer and Tisdall.[16]

20. Scudder, J.; Zwemer, R. L., and Whipple, A. O.: Acute Intestinal Obstruction: Evaluation of Results in Two Thousand One Hundred and Fifty Cases, with Detailed Studies of Twenty-Five Showing Potassium as a Toxic Factor, Ann. Surg. **107**:161-197 (Feb.) 1938.

21. Keith, N. M., and Binger, M. W.: Diuretic Action of Potassium Salts, J. A. M. A. **105**:1584-1590 (Nov. 16) 1935.

most loop of the jejunum was completely obstructed. These dogs lived five, six and eight days respectively before severe intoxication occurred. During these periods, other alterations in the constituents of the blood, such as azotemia, hypochloremia, alkalosis and dehydration, were observed; in all 3 dogs the concentration of the sodium and total bases

TABLE 2.—*Changes in Constituents of the Blood Following High Jejunal Obstruction*

Dog	Day	Blood Urea, Mg. per 100 Cc.	Plasma NaCl, Mg. per 100 Cc.	Plasma CO_2-Combining Power, Vol. %	Serum Na, Mg. per 100 Cc.	Serum K, Mg. per 100 Cc.	Serum Ca, Mg. per 100 Cc.	Serum Protein, Gm. per 100 Cc.	Total Base, Cc. N/10 NaOH	Hematocrit, per Cent
1	Before	30	619	50.4	354	29.0	11.3	...	170	46
	1	16	632	46.6	348	33.2	11.2	6.9	...	52
	2	28	597	50.4	342	37.6	11.2	...	...	42
	3	16	573	49.4	331	37.3	10.2	...	...	46
	4	24	...	....	308	36.7	11.4	...	...	41
	5	..	....	....	...	....	....	...	...	..
	6	24	491	56.0	296	30.2	10.4	...	...	45
	7	..	...	....	...	....	....	...	...	..
	8	24	468	71.0	308	36.9	9.4	6.9	151	51
2	Before	26	679	46.6	336	20.9	9.8	6.1	160	38
	1	22	573	47.5	331	19.3	9.2	...	...	40
	2	54	556	54.1	342	24.4	11.8	...	...	44
	3	..	...	....	...	....	....	...	...	..
	4	34	456	57.9	325	25.0	11.0	...	...	43
	5	44	421	62.6	290	23.0	9.6	...	...	40
	6	88	398	49.0	308	34.1	10.6	8.5	151	50
3	Before	27	644	44.7	339	24.1	13.8	8.7	172	57
	1	16	544	46.7	347	25.3	11.3	...	...	57
	2	18	528	57.0	336	27.0	8.1	...	...	..
	3	22	480	62.6	313	28.4	6.9	...	...	56
	4	68	456	....	296	42.6	11.8	...	...	63
	5	186	412	46.6	307	38.3	12.4	9.2	150	59

TABLE 3.—*Comparison of the Distribution of Sodium and Potassium in the Blood of Man, Dogs and Cats*

	Cells		Plasma	
	Sodium, Mg. per 100 Cc.	Potassium, Mg. per 100 Cc.	Sodium, Mg. per 100 Cc.	Potassium, Mg. per 100 Cc.
Man	22	408	313	19
Man	27	415	331	17
Dog	208	20	342	20
Dog	211	17	330	17
Cat	337	38	388	32
Cat	217	41	336	34

of the serum decreased greatly, whereas the concentration of calcium in the serum tended to remain within normal limits. However, in contrasting the behavior of the serum potassium during obstruction in human beings and in animals, it must be remembered that the distribution of sodium and potassium between the cells and the plasma of the blood differs vastly in the two groups. Table 3 shows that whereas in dogs and cats there is the same concentration of potassium in the cells as in the plasma, in human beings the concentration of potassium in

the cells is twenty times that in the plasma, and the relation of sodium to potassium in the blood cells in man is just the opposite of that in experimental animals. These facts make it difficult to presume that the potassium of the blood has the same function in the economy of the animal that it has in that of human beings.

FACTORS AFFECTING THE SERUM POTASSIUM DURING INTESTINAL OBSTRUCTION IN MAN

It is obvious from a perusal of our findings in clinical cases that, because alterations in the concentration of serum potassium during obstruction do not occur constantly, they are secondary to other factors. Indeed, all the changes which occur in the constituents of the blood during obstruction appear to be secondary to the onset of clinical intoxication and exert but a contributory influence on the fatal termination.[22] When one considers the mechanism by which the decrease in the concentration of potassium in the serum is brought about, three possible factors present themselves. These will now be dealt with in turn.

TABLE 4.—*Composition of the Secretions Aspirated from the Stomach in Clinical Cases of Intestinal Obstruction*

	Case									
	1	2	3	4	5	6	7	8	9	10
Volume for 24 hours, cc.	2,500	2,250	1,900	1,750	1,350	1,230	1,080	1,000	860	670
Cl content, mg. per 100 cc.	514	271	191	169	377	226	194	375	371	497
Na content, mg. per 100 cc.	256	135	164	115	267	164	55	112	129	213
K content, mg. per 100 cc.	83	28	57	43	89	62	41	52	51	44

The first and probably the most potent factor is the great loss of potassium from the body which occurs as the result of vomiting or aspiration of retained gastric contents. This observation has been noted previously by Scudder and his associates.[23] Table 4 contains some data concerning the amounts of potassium which may be lost in the course of twenty-four hours in cases in which continuous gastric aspiration is employed. In spite of sips of water by mouth, the concentration of potassium in specimens of the gastric contents was two to four times that in the serum. The stomach is responsible for this active loss of potassium (table 5), because the gastric secretions alone have a high content of potassium, whereas the remaining gastrointestinal secretions, including the succus entericus,[24] have lower concentrations of potassium. It is

22. Falconer, M. A.: Clinical Aspects of the Blood Chemistry in Intestinal Obstruction, Proc. Staff Meet., Mayo Clin. **13**:460-464 (July 20) 1938.

23. Scudder, Zwemer and Truszkowski.[5] Scudder, Zwemer and Whipple.[20]

24. de Beer, E. J.; Johnston, C. G., and Wilson, D. W.: The Composition of Intestinal Secretions, J. Biol. Chem. **108**:113-120 (Jan.) 1935.

interesting to note that this same factor of loss of potassium in the gastric contents during obstruction has been observed in cats by Scudder [5] and his associates and in dogs by us.

The second factor for consideration is the possible antagonism of sodium and potassium in the blood, as was first suggested by Bunge in 1873.[25] The majority of our subjects were given solutions of sodium chloride intravenously, and often the concentration of potassium in the serum continued to decrease after saline therapy was instituted, especially in cases (cases 8, 13, 25, 26 and 27) in which gastric or duodenal suction was continued. Although both Scudder [20] and we observed low concentrations of serum potassium before treatment was commenced, we performed the following experiments in order to test this possibility.

The principle on which our experiments were based was to give a healthy male volunteer large amounts of sodium chloride, at the same time restricting his intake of potassium, in order to ascertain the effect

TABLE 5.—*Composition of Normal Digestive Secretions (Four Examples of Each)*

	Fasting Stomach Secretions				Fasting Duodenal Secretions				T Tube Bile			
Cl content, mg. per 100 cc.	422	401	292	248	404	376	269	222	407	357	342	336
Na content, mg. per 100 cc.	9	37	181	181	292	240	191	142	309	298	306	361
K content, mg. per 100 cc.	93	98	107	49	20	17	29	20	10	9	9	20

on the concentration of potassium in the serum. Throughout the periods of observation our subject continued at his work, and after 1 experiment a period of a month was allowed to elapse before a second experiment was begun. We first administered a diet low in potassium, prepared according to the methods of Sister Mary Victor [26] and containing known amounts of potassium with an energy content of at least 2,200 calories per day. The results are summarized in table 6. This regimen was without significant effect on the values for serum potassium, the hematocrit indexes of the blood or the weight. In our second experiment the same diet was used and, in addition, 1,000 cc. daily of a solution of 2 per cent sodium chloride was given intravenously (table 7). The concentration of potassium decreased within three days to 15.5 mg. per hundred cubic centimeters of serum, but with continued administration of saline solution we were unable to depress it further. In addition, the

25. Bunge, G.: Ueber die Bedeutung des Kochsalzes und das Verhalten der Kalisalze im menschlichen Organismus, Ztschr. f. Biol. **9**:104-143, 1873.

26. Mary Victor, Sister: Directions for the Planning and Preparation of Diets Low in Content of Potassium, Proc. Staff Meet., Mayo Clin. **12**:424-432 (July 7) 1937.

hematocrit indexes decreased considerably, and our subject showed a tendency to gain weight, the signs of both being evidence of retention of water. The decrease noted in the concentration of potassium in the serum, therefore, cannot be ascribed entirely to the antagonism of an

TABLE 6.—*Effect on the Chemical Constituents of the Blood of a Low Potassium Diet (Normal Male Adult)*

	Examination of Blood						Urine			
Day	Plasma NaCl, Mg. per 100 Cc.	Serum Na, Mg. per 100 Cc.	Serum K, Mg. per 100 Cc.	Serum Ca, Mg. per 100 Cc.	Hematocrit, per Cent	Weight, Pounds	Vol., Cc.	NaCl, Gm.	Na, Gm.	K, Gm.
				On Normal Diet						
1	627	325	17.6	10.3	46	164½	750	8.7	3.2	3.2
2	629	342	20.0	10.6	44	164½	700	10.1	3.3	2.7
3	627	325	18.3	10.2	46	164	1,470	7.2	2.1	2.3
				On Low Potassium Diet (1.7 Gm. K)						
4	581	331	18.3	9.8	46	163	720	9.8	3.3	3.2
5	623	331	18.0	9.9	44	162½	800	11.6	3.2	2.3
6	585	308	18.0	9.9	45	162	500	8.3	2.3	1.7
7	597	325	17.5	10.1	43	162½	610	7.9	2.7	1.3
				On Low Potassium Diet (0.8 Gm. K)						
8	644	345	18.4	10.2	44	162	620	5.9	1.3	1.3
9	594	334	19.0	10.9	44	162	570	4.8	1.7	1.7

TABLE 7.—*Effect on the Chemical Constituents of the Blood of Repeated Intravenous Infusion of Sodium Chloride Solution* *

	Examination of Blood						Urine			
Day	Plasma NaCl, Mg. per 100 Cc.	Serum Na, Mg. per 100 Cc.	Serum K, Mg. per 100 Cc.	Serum Ca, Mg. per 100 Cc.	Hematocrit, per Cent	Weight, Pounds	Vol., Cc.	NaCl, Gm.	Na, Gm.	K, Gm.
				On Normal Diet						
1	623	325	20.7	9.7	48	164½	650	9.5	1.5	2.2
2	627	336	18.9	9.9	48	164½	830	6.8	1.9	2.8
3	609	354	22.4	9.8	48	164	620	7.6	1.4	2.0
4	683	359	20.0	11.3	45	164	640	8.2	1.3	1.8
				On Low Potassium Diet (1.7 Gm. K) with 1,000 Cc. 2% NaCl Intravenously						
5	660	336	18.7	10.1	44	165½	1,280	20.7	3.0	2.9
6	635	342	17.0	9.8	42	165	2,400	30.7	5.6	1.8
7	644	328	15.5	9.9	43	166	1,250	23.5	2.9	0.8
8	660	331	15.6	9.6	40	167½	1,300	29.2	3.2	1.5
				On Low Potassium Diet (0.8 Gm. K) with 1,000 Cc. 2% NaCl Intravenously						
9	619	331	16.2	9.8	..	167½	1,420	23.9	3.3	0.9
10	651	319	15.3	9.4	41	167	1,530	27.1	3.5	0.8

* Same subject as in table 6.

excess intake of sodium, because dilution of the serum as a result of retention of water probably played a part. In a third experiment, 2 per cent Ringer's solution (sodium chloride 1.85 per cent, potassium chloride 0.10 per cent and calcium chloride 0.05 per cent) was substituted for the simple solution of sodium chloride (table 8), and there was only a slight decrease in the concentration of potassium in the serum and no significant change in the hematocrit readings or in the weight.

We deduced from these observations that although the administration of large amounts of a solution of sodium chloride will cause a slight decrease in the concentration of potassium in the blood, continued or repeated administration will not depress it further. Harrop,[27] in a review of the literature on the subject, arrived at the same conclusion. We made two other deductions: first, the addition of small quantities of potassium, as in Ringer's solution, was sufficient to protect the normal level of serum potassium from the effect of administration of sodium chloride; second, administration of Ringer's solution intravenously is less likely to lead to retention of water than is administration of simple solutions of sodium chloride. The latter opinion has been

TABLE 8.—*Effect on the Chemical Constituents of the Blood of Repeated Intravenous Infusion of Ringer's Solution* *

	Examination of the Blood						
Day	Plasma NaCl, Mg. per 100 Cc.	Serum Na, Mg. per 100 Cc.	Serum K, Mg. per 100 Cc.	Serum Ca, Mg. per 100 Cc.	Hematocrit, per Cent	Weight, Pounds	Urine Volume, Cc.
			On Normal Diet				
1	611	319	20.0	9.8	46	163	900
	On Low Potassium Diet (1.7 Gm. K) with 1,000 Cc. 2% Ringer's Solution Intravenously						
2	627	313	19.5	9.3	44	163½	920
3	594	325	17.9	9.4	44	163½	1,150
4	627	319	15.8	9.2	43	163½	1,180
5	635	319	17.0	9.0	44	163	1,220
	On Low Potassium Diet (0.8 Gm. K) with 1,000 Cc. 2% Ringer's Solution Intravenously						
6	602	319	18.3	9.4	43	163	1,190
7	643	313	16.6	9.3	44	162½	1,140

* Same subject as in table 6.

expressed also by Coller, Dick and Maddock.[28] Similar findings resulted from a series of observations we made on patients recovering from operations on the stomach, to whom large amounts of a solution of sodium chloride were given intravenously each day and to whom only small sips of water were given by mouth. Among these patients the concentration of potassium in the serum would fall during a period of three or four days, but only to the extent of a few milligrams. Control observations of patients who were taking food by mouth did not show any significant results.

27. Harrop, G. A.: The Water and Salt Hormone of the Adrenal Cortex, Bull. Johns Hopkins Hosp. **59**:25-34 (July) 1936.

28. Coller, F. A.; Dick, V. S., and Maddock, W. G.: Maintenance of Normal Water Exchange with Intravenous Fluids, J. A. M. A. **107**:1522-1527 (Nov. 7) 1936.

It would seem, then, that in cases of obstruction in which a decrease in the concentration of serum potassium occurred during administration of saline therapy, the most potent factor in the mechanism of this decrease was the continued loss of potassium by the body by way of the aspirated gastric contents.

A third factor, possibly active in a few cases, was suggested to us by the observation of Aitken and his associates,[29] who found that the administration of dextrose to a patient suffering from familial periodic paralysis would depress the concentration of potassium to 12 mg. per hundred cubic centimeters of serum or less and would initiate an attack of paralysis. Because dextrose solutions had been given simultaneously with saline solutions to many of our patients, we selected 1 patient (case 26) for whom the concentration of potassium had been 9.5 mg.

TABLE 9.—*Dextrose-Potassium Tolerance Test*

Time	Case 26			Control		
	Blood Sugar, Mg. per 100 Cc.	Serum K, Mg. per 100 Cc.	Serum Na, Mg. per 100 Cc.	Blood Sugar, Mg. per 100 Cc.	Serum K, Mg. per 100 Cc.	Serum Na, Mg. per 100 Cc.
Before ingestion of dextrose.....	101	17.7	319	83	19.0	324
250 Gm. dextrose ingested by mouth						
1 hour later.....	361	15.0	310	146	18.2	319
3 hours later.....	326	14.5	313	90	18.0	319
5 hours later.....	230	15.9	310	59	17.8	319

per hundred cubic centimeters of serum when obstruction was present. We gave her 250 Gm. of dextrose, following the directions of Aitken and his co-workers. The result is tabulated in table 9. Under circumstances similar to these, in Aitken's case the concentration of potassium fell to less than 8 mg. per hundred cubic centimeters of serum and remained stationary at that level until potassium chloride was given by mouth. Because no such decrease occurred in our patient and because the concentration of potassium in the serum showed a spontaneous tendency toward recovery, we presumed that the administration of dextrose was not a factor in the decrease in concentration of serum potassium previously noted in her case.

We may conclude from consideration of the three factors we have reviewed that loss of potassium in the gastric secretions is the most potent factor and that it is the only one operating in all cases.

29. Aitken, R. S.; Allott, E. N.; Castleden, L. I. M., and Walker, M.: Observations on a Case of Familial Periodic Paralysis, Clin. Sc. **3**:47-57 (July 6) 1937.

SIGNIFICANCE OF OUR OBSERVATIONS AS REGARDS THERAPY

Although the need for saline solutions as adjuncts in the treatment of intestinal obstruction is widely recognized, less attention has been paid to the composition of the solutions which should be employed. One of the results of this investigation has been to focus attention on the need for small quantities of potassium and calcium, in addition to sodium, in the infusion fluids.

We have shown that in man there is a tendency for the concentrations of each of the three principal bases of the serum to decrease and that this decrease is usually most apparent in the concentration of potassium. The total amount of sodium lost from the body as the result of vomiting and distention of the obstructed loops of bowel is greater than the amount of potassium lost; because sodium is present in the serum in much larger amounts than potassium, however, loss of sodium has less effect on the chemical constituents of the blood than has loss of comparable amounts of potassium. This observation that the concentration of all three bases, sodium, potassium and calcium, tends to fall suggests to us that it is more logical to employ solutions containing potassium and calcium, such as Ringer's solution, in the treatment of intestinal obstruction than it is to use solutions containing sodium chloride alone.

This contention is difficult to prove, because we have not been able to correlate any symptoms with the low levels of potassium and calcium observed and because the administration of simple saline solutions gives good results in the majority of cases. We have not seen any instances of muscular paralysis or tetany in this series of cases. On the other hand, 3 patients for whom the concentration of potassium in the serum was low received potassium and calcium salts together with sodium in the infusion fluids, with, we think, some benefit. The first 2 (cases 25 and 26) were suffering from languor following paralytic intestinal obstruction; in both the symptoms of obstruction had been relieved for several days but without correction of languor and weakness, and in both the addition of potassium and calcium salts to the solution of sodium chloride was accompanied by a simultaneous improvement in the condition. In the third case (case 27) paralytic ileus and severe vomiting of the retention type had been present for five days without signs of amelioration. The addition of calcium salts on the fifth day was without apparent effect, but on the succeeding day the administration of potassium and calcium salts was followed within a few hours by cessation of the vomiting. In all 3 cases, increase in the concentration of bases of the serum to normal levels occurred on recovery.

Such quantities of potassium and calcium as are contained in Ringer's solution are probably ample for the routine treatment of

intestinal obstruction, as is evidenced by case 8, in which, in spite of a severe degree of retention (as much as 2,400 cc. daily), no significant depression occurred in the concentration of potassium in the serum. In a few cases, such as the 3 mentioned, it might be better if larger proportions of potassium and calcium are used. In addition to these theoretic advantages of the use of Ringer's solution, there is the important fact that administration of Ringer's solution is less likely to lead to retention of water than is the administration of a simple solution of sodium chloride.

CONCLUSIONS

We have been unable to verify the idea that hyperpotassemia or hypercalcemia, both of which are known to occur in experimental studies on animals, are present in cases of clinical obstruction in man. Indeed, our observations lead us to believe that during clinical obstruction there is a tendency for the concentration of bases in the serum to decrease and that the concentration of potassium in the serum decreases relatively more than either that of sodium or that of calcium. The mechanism which causes this fall in the potassium content of the serum is probably one of active secretion of potassium into the gastric contents, which potassium is then lost by the body through the mechanism of vomiting or gastric aspiration. These findings suggest to us that infusion fluids, such as Ringer's solution, which contain small quantities of potassium and calcium salts in addition to sodium should be used in the routine treatment of intestinal obstruction.

EFFECTS ON KIDNEY AND BLOOD PRESSURE OF ARTIFICIAL COMMUNICATION BETWEEN RENAL ARTERY AND VEIN

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Experimental studies on hypertension have demonstrated that in dogs an elevation of blood pressure can be produced and maintained by constricting the renal artery and decreasing the flow of blood through the kidney.[1] We have reported a series of experiments in which we employed Goldblatt's method of producing hypertension. In the course of this experimental work it occurred to us that the flow of blood through the kidneys might be diminished by constructing an artificial opening between the renal artery and the renal vein so that part of the arterial blood would be diverted into the vein without passing through the kidney.

Since Carrel published his description[2] of a uniformly satisfactory technic for making a vascular anastomosis, studies of the effects of experimentally produced arteriovenous fistulas have been reported by many authors. Two instances of this lesion between the renal vessels in human subjects have been reported,[3] but we have been unable to find any recorded observations of a similar condition in the experimental animal. We therefore contribute a study of the technic required to anastomose these vessels successfully and of certain of the pathologic and physiologic effects of the lesion on the kidney and on the organism as a whole.

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From the Department of Surgery of the New York Hospital and Cornell University Medical College.

1. Goldblatt, H.; Lynch, J.; Hanzal, R. F., and Summerville, W. W.: Studies on Experimental Hypertension: I. The Production of Persistent Elevation of Systolic Blood Pressure by Means of Renal Ischemia, J. Exper. Med. **59**:347, 1934.

2. Carrel, A.: La technique opératoire des anastomoses vasculaires et de la transplantation des viscères, Lyon méd. **93**:859, 1902; The Surgery of Blood Vessels, Bull. Johns Hopkins Hosp. **18**:18, 1907.

3. Varela, M. E.: Aneurisma arterio venoso de las vasos renales y asistolia consecutiva, Rev. méd. latino-am. **157**:3244, 1928. Camp, F. B.: Personal communication to the authors.

METHODS

Carotid loops [4] were constructed in male dogs of varying sizes, and after a series of daily observations had been made to establish the average normal systolic blood pressure and pulse rate an arteriovenous fistula was created between the renal vessels. Daily determinations of the urea nitrogen content of the blood gave an indication of the functional ability of the renal substance distal to these communications.

Recent publications on surgical management of the blood vessels stress the necessity of approximating the intima of one vessel to that of the other. The methods of accomplishing this are well known. Of almost equal importance is the exclusion of blood and tissue juices from the immediate field of operation. That adequate exposure of the vessels must be secured is obvious. The procedure to be described fulfils these requirements.

The dog, anesthetized with pentobarbital sodium given intravenously, is placed on the table on its side, with a large sand bag under the dependent lumbar region. The skin of the entire flank is shaved and prepared in the usual manner, and a rectangular field just below and parallel to the last rib is draped with sterile towels. The incision should be 9 to 10 cm. long and is made parallel to the last rib and about 2 cm. below it. When the right renal vessels are to be exposed, the rib is resected subperiosteally from its angle to the costal cartilage. This is not necessary on the left side. The original incision is carried through the oblique and transversus muscles and their fused tendons posteriorly. The parietal peritoneum is pushed forward and the perirenal space entered. The renal fascia is incised, and the kidney is freed from its bed by blunt dissection and delivered into the wound. The peritoneum is gently peeled from the anterior surface of the kidney and its pedicle, and the wound is lined with moist Mikulicz pads. With the kidney tilted forward toward the dog's abdomen, the posterior aspect of the vessels may be freed from all other structures. The kidney is then tilted toward the animal's back, and the remaining surfaces of the artery and vein are dissected free. A Beard lid clamp with rubber-shod tips is loosely applied to both artery and vein as close to the vena cava as possible. At the hilus the vessels are occluded by means of a flexible-tipped, rubber-shod artery forceps (fig. 1). The clamps must not be so tightly applied as to injure seriously the walls of the artery or vein. With the posterior aspect of the vessels in view, all other structures are packed out of the way with strips of silk cloth soaked in a solution of 3 parts petrolatum and 1 part liquid petrolatum.

With a curved bistoury a longitudinal incision is made into the wall of the vein which is apposed to the artery, and the incision is lengthened to the desired size with small sharp scissors. The lumen is immediately washed with saline solution at 40 C. An incision the mirror image of this is now made in the artery, and with tiny toothed forceps and a knife the adventitia is stripped back from the edges of the opening. Both wounds are lightly coated with a warm solution of petrolatum and mineral oil. With Deknatel's finest arterial silk soaked in petrolatum and threaded on Kalt's smallest curved corneal needles, stay sutures are so placed and tied (fig. 1) as to bring the ends of the venous and arterial defects together. With the aid of a temporary tension suture midway between the stay sutures (fig. 2) the long end of one of the latter is used as a running stitch to

4. Child, C. G., and Glenn, F.: Modification of Van Leersum Carotid Loop for Determination of Systolic Blood Pressure in Dogs, Arch. Surg. **36**:381 (March) 1938.

approximate the posterior walls of the artery and the vein. When the suture line is completed, the silk is tied to the short end of the second stay suture, and the position of the kidney is reversed so as to bring the anterior aspect of the vessels into view. The strips of silk cloth are rearranged, and the edges of the opening and the posterior suture line are washed with saline solution and coated with petrolatum-oil solution. The long end of the second stay suture brings the anterior walls of the vessels together in a running stitch. The closure of the

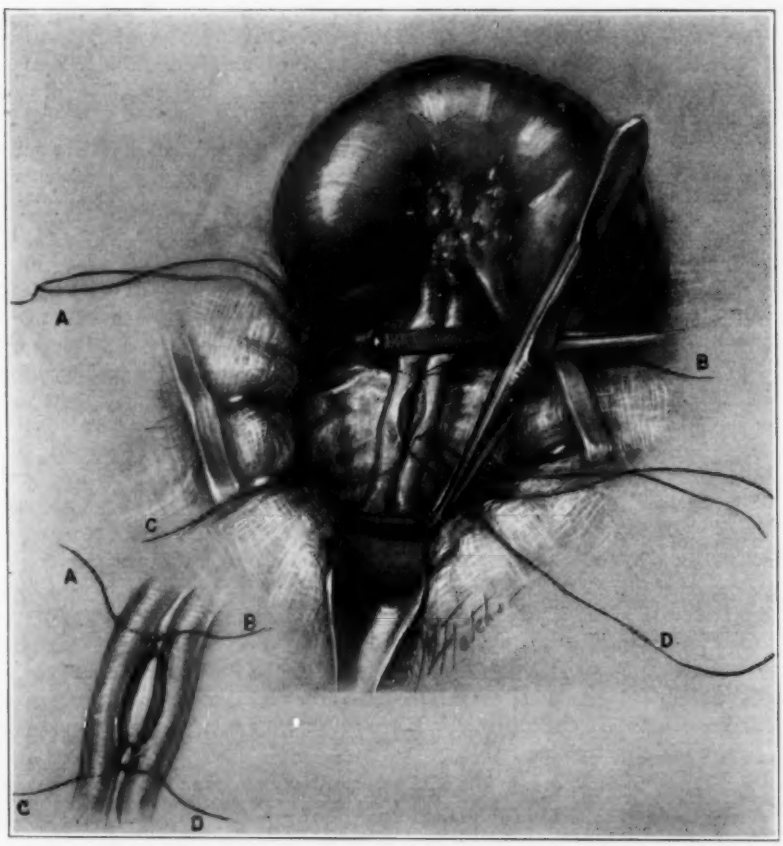

Fig. 1.—Drawing to show the exposure gained and the manner in which the clamps are placed and the vessels opened. The inset shows the method of tying the stay sutures so as to evert the edges of the artery and vein.

stoma is completed by tying this suture to the short end of the first stay suture. In placing the sutures in the vessels it is to be remembered that the smaller the everted margin the less will be the likelihood of constriction of either the artery or the vein at the site of the fistula. With sponges saturated in warm saline solution packed about the suture lines, the clamp at the hilus is removed. It is not usually necessary to deprive the kidney of its blood supply for more than thirty-five or forty minutes while the fistula is being made.

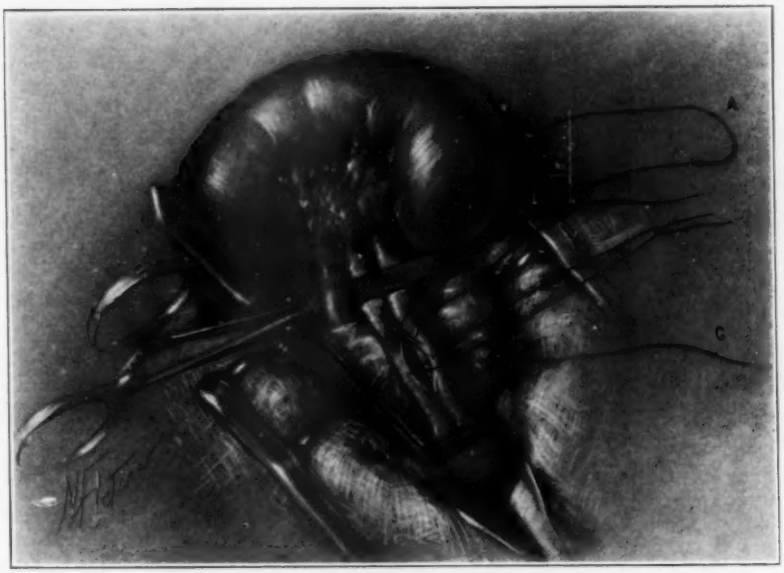

Fig. 2.—Opposite side of the pedicle from that seen in figure 1, showing the completed posterior suture line and the position of the temporary tension suture.

Fig. 3.—Completed anastomosis. The distention of the vein at the fistula is apparent. There is no constriction of the vessels due to suturing.

The downward rush of blood forces out between the sutures the small amount of air that may have been enclosed within the vessels. The Beard clamp is then removed, and within a few seconds the kidney assumes a lighter hue, though it never regains its original color. After a few minutes the packs are removed and the anastomosis inspected. The churning of arterial blood within the distended vein is clearly apparent (fig. 3), and a strong thrill can be felt over the vessels and the hilus of the kidney. The kidney is then replaced, with care not to kink the pedicle, and the operation is completed by closing the wound in layers with interrupted sutures of silk in the muscles and running intracutaneous or interrupted sutures in the skin. A simple collodion-gauze dressing is applied over the operative field.

In this manner artificial communications between the renal artery and the renal vein have been fashioned in 12 dogs, and all but 1 (experiment 9) of the fistulas have remained patent throughout the period of observation. The average length of the fistula, as measured at the time of operation, was 1 cm. In 2 dogs (experiments 5 and 7) with larger fistulas a thrill was felt over the flank, and in all instances in which the fistula was patent a bruit was audible.

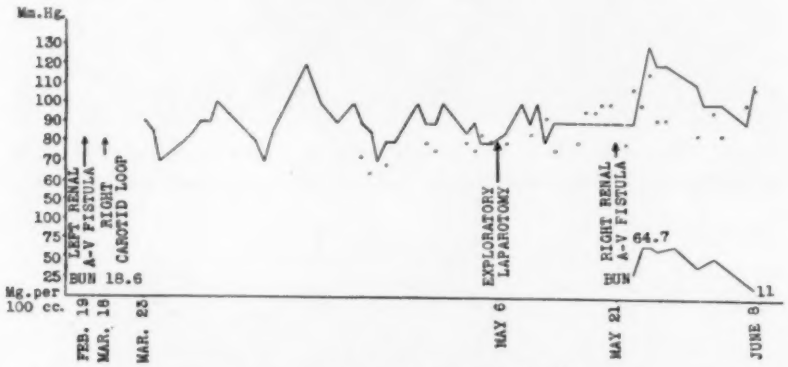

Fig. 4 (experiment 1).—Transient rise in the pulse, blood pressure and urea nitrogen content of the blood after the formation of the second fistula. (As in the three following figures the lower line represents the level of the urea nitrogen. The upper line is a graph of the systolic blood pressure. The circles represent the pulse rate.)

Detailed protocols of the experiments are here presented. Protocols in tabulated form, together with pathologic reports, will be found at the end of the article.

PROTOCOLS

Experiment 1.—In a male dog weighing 26½ pounds (12.2 Kg.) a left renal arteriovenous fistula 8 mm. long was made on Feb. 19, 1938. On Feb. 21 the urea nitrogen content of the blood was 18.6 mg. per hundred cubic centimeters. A right carotid loop was fashioned on March 18, and between March 23 and May 20 the average daily blood pressure was 95 and the pulse rate 80. An exploratory laparotomy on May 6 revealed the fistula to be patent. On May 21 an arteriovenous fistula 9 mm. long was made in the right kidney. The blood pressure rose to 130 by the fourth postoperative day, and the pulse rate to 116 (fig. 4). The urea nitrogen content of the blood rose gradually to 64.7 by the third postoperative

day and remained approximately at this level for ten days. The blood pressure had fallen to 100 and the pulse rate to 96 by the twelfth postoperative day and have remained at these levels to the present time. The value for urea nitrogen on the seventeenth postoperative day was 11 mg. The dog is alive and well. A bruit can be heard over each flank.

Experiment 2.—In a male dog weighing 30 pounds (13.6 Kg.) a left renal arteriovenous fistula 1 cm. long was made on Feb. 7, 1938. Four days later a right carotid loop was fashioned, and from February 17 to February 28 the average daily blood pressure was 100. The value for urea nitrogen on February 14 was 17 mg. An arteriovenous fistula 1 cm. long was made in the left kidney February 28, and uremia developed, proving fatal on March 4. The blood pressure was 160 during the first two postoperative days and 145 the day before death. The value for urea nitrogen rose rapidly and was 136 on the morning of the day on which the animal died.

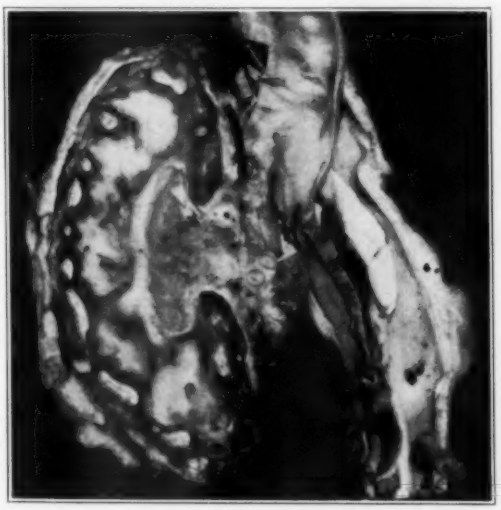

Fig. 5 (experiment 2).—Right kidney twenty-five days after formation of a renal arteriovenous fistula. The organ is very small and is composed of islets of pale necrotic material containing calcium separated by bands of fibrous tissue and fat. A bristle lies in the communication between the vessels.

Experiment 3.—In a male dog weighing 31 pounds (14.1 Kg.) a right renal arteriovenous fistula 1 cm. long was made on Feb. 18, 1938. After the formation of a right carotid loop on February 25, the animal's blood pressure on March 7 was found to be 150 and the urea nitrogen content of the blood 19.4 mg. per hundred cubic centimeters. After a right nephrectomy on March 7 the dog had uremia and died in four days. The blood pressure was 170 on the third postoperative day but did not rise above 140 on the other days. The value for urea nitrogen rose progressively, reaching 162.3 mg. per hundred cubic centimeters about six hours before death (fig. 6).

Experiment 4.—In a male dog weighing 36 pounds (16.3 Kg.) a right carotid loop was constructed on March 8, 1938, and between March 12 and March 19 the average daily blood pressure was 120. A right renal arteriovenous fistula 1 cm.

long was made on March 19, and for three days thereafter there was a slight rise in the urea nitrogen content of the blood but no significant change in the blood pressure. An intravenous pyelogram on March 30 resulted in visualization of the left urinary tract only. The dog died of distemper eighteen days after the formation of the fistula. The opening was patent and measured 4 mm. in diameter.

Experiment 5.—In a male dog weighing 41½ pounds (19 Kg.) a right carotid loop was fashioned on March 21, 1938. The average daily blood pressure between March 26 and April 2 was 110, and an intravenous pyelogram on March 30 was effective in visualizing the urinary tract on both sides. A right renal arteriovenous fistula 1.2 cm. long was made on April 2. No elevation of blood pressure or of the urea nitrogen content of the blood followed this, and on April 20 an arteriovenous fistula 1.8 cm. long was made in the left kidney. An intravenous pyelogram

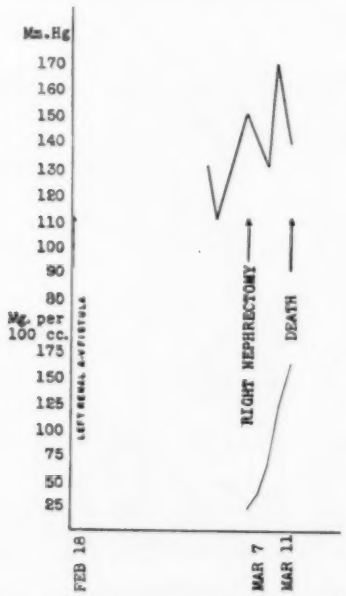

Fig. 6 (experiment 3).—The removal of the normal kidney opposite to the side on which a renal arteriovenous fistula has been made is shown to result in a progressive increase in the urea nitrogen content of the blood and a slight transient rise in the systolic blood pressure.

the next day did not visualize the urinary tract on either side. The dog's blood pressure rose gradually, as did the pulse rate, the former being 150 on March 23 and the latter 96. The animal died of uremia, with a urea nitrogen content of the blood of 204.5 mg. per hundred cubic centimeters on the fifth postoperative day.

Experiment 6.—In a male dog weighing 40 pounds (18.1 Kg.) a right carotid loop was made on March 21, 1938, and the average daily blood pressure between March 28 and April 8 was 110. An intravenous pyelogram on March 30 successfully visualized both urinary tracts. On April 8 a right renal arteriovenous fistula 2 cm. long was made. This was followed by a slight rise in the urea nitrogen of the blood and the pulse rate and a fall in the blood pressure, the respective levels being 22.4 mg., 140 and 90. Bilateral cutaneous ureterostomies were formed on April 15, and on the following day catheters were inserted and a differential phenol-

sulfonphthalein test done, showing 10 per cent less excretion of the dye on the right in one hour. The right kidney excreted 18 cc. of urine in forty-three minutes and the left 36 cc. That excreted on the right contained 0.82 Gm. of urea nitrogen per liter and that on the left 9.3 Gm. Three days later the animal succumbed to bilateral pyelonephritis. The value for urea nitrogen on April 18 was 109 mg. per hundred cubic centimeters of blood.

Experiment 7.—In a male dog weighing 46 pounds (20.9 Kg.) a right carotid loop was constructed on March 22, 1938. An intravenous pyelogram on March 30 was effective in visualizing both urinary tracts. The average daily blood pressure between March 31 and April 8 was 100. A right renal arteriovenous fistula 1.5 cm. long was made on April 9, and two days later the urea nitrogen content of the blood was 17.3 mg. per hundred cubic centimeters, the blood pressure 110 and

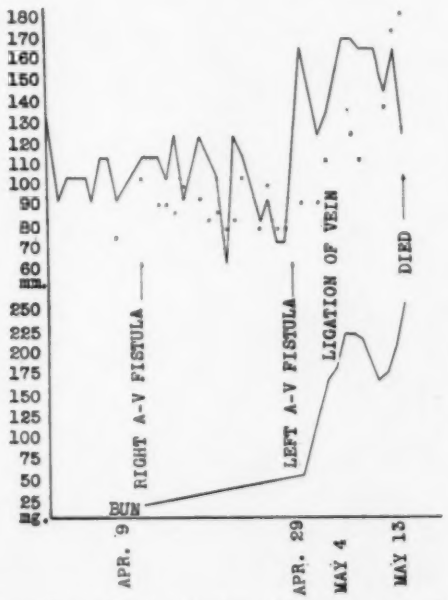

Fig. 7 (experiment 7).—Chart showing the manner in which the mild hypertension produced by the formation of the second fistula is accompanied by a rise in the pulse rate and the urea nitrogen content of the blood. A transient decrease in the last followed the ligation of the left renal vein between the fistula and the vena cava.

the pulse rate 100. An intravenous pyelogram on April 21 effected visualization on the left side only. On April 29 a left renal arteriovenous fistula 7 mm. long was made. The changes which followed this are clearly shown in figure 9. Thirteen days after the formation of the second fistula the animal died in uremia, the urea nitrogen content of the blood being 252.4 mg. per hundred cubic centimeters.

Experiment 8.—In a male dog weighing 42 pounds (19.1 Kg.) a right carotid loop was fashioned on March 21, 1938, and daily determinations of the blood pressure between April 7 and April 25 established an average level of 110. An intravenous pyelogram on April 21 visualized both urinary tracts. On April 24 a right renal arteriovenous fistula 1.2 cm. long was made, and a rise of the blood pressure to 160 appeared in two days, though the value for urea nitrogen was

only 19.9 mg. per hundred cubic centimeters. The construction of a left renal arteriovenous fistula 8 mm. in length on May 6 was followed by a further rise in blood pressure to a peak of 205 on the sixth postoperative day. After the formation of the first fistula the pulse rate did not vary significantly from an average of 100. The dog died in a uremic convulsion (value for nitrogen, 266.4 mg. per hundred cubic centimeters of blood) seven days after the second fistula was established.

Experiment 9.—In a male dog weighing 31½ pounds (14.2 Kg.) a right carotid loop was constructed on March 25, 1938. The average daily blood pressure between March 31 and April 9 was 90. On April 29 a right renal arteriovenous fistula 1 cm. long was made. A transient rise in blood pressure, reaching a peak of 160 on the fourth postoperative day, appeared after this, but only a slight rise in pulse rate occurred, and the value for urea nitrogen in the blood on May 2 was

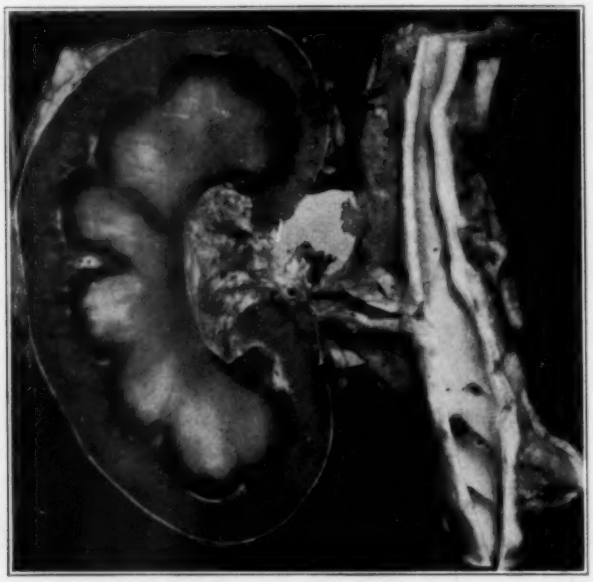

Fig. 8 (experiment 8).—Right kidney eighteen days after formation of a renal arteriovenous fistula. The organ is slightly reduced in size. The cortex is pinkish yellow, the medulla light yellow and the region of the arcuate vessels dark red.

14.9 mg. per hundred cubic centimeters. After May 26 a bruit could not be heard, and since no permanent change in the vital signs had been produced the animal was killed by means of an overdose of chloroform on June 16.

Experiment 10.—In a male dog weighing 41 pounds (18.6 Kg.) a right carotid loop was fashioned on May 14, 1938. The average daily blood pressure between May 19 and June 2 was 100 and the pulse 72. On June 2 a right renal arteriovenous fistula 11 mm. long was made. This was followed by transient tachycardia but by no change in the systolic tension. Fourteen days later the animal was killed and the aorta injected with Hill's solution.[5] A rich collateral circulation was revealed, arising chiefly from the right ureteral, spermatic and lowest intercostal vessels.

5. Hill, E. C.: Notes on an Opaque X-Ray Mass, Bull. Johns Hopkins Hosp. **35**:218, 1924.

Experiment 11.—In a male dog weighing 37½ pounds (17 Kg.) a right carotid loop was made on April 22, 1938. The average daily blood pressure between April 29 and May 20 was 120 and the pulse rate 70. The establishment of a right renal arteriovenous fistula 1 cm. long on May 24 was followed by a slight

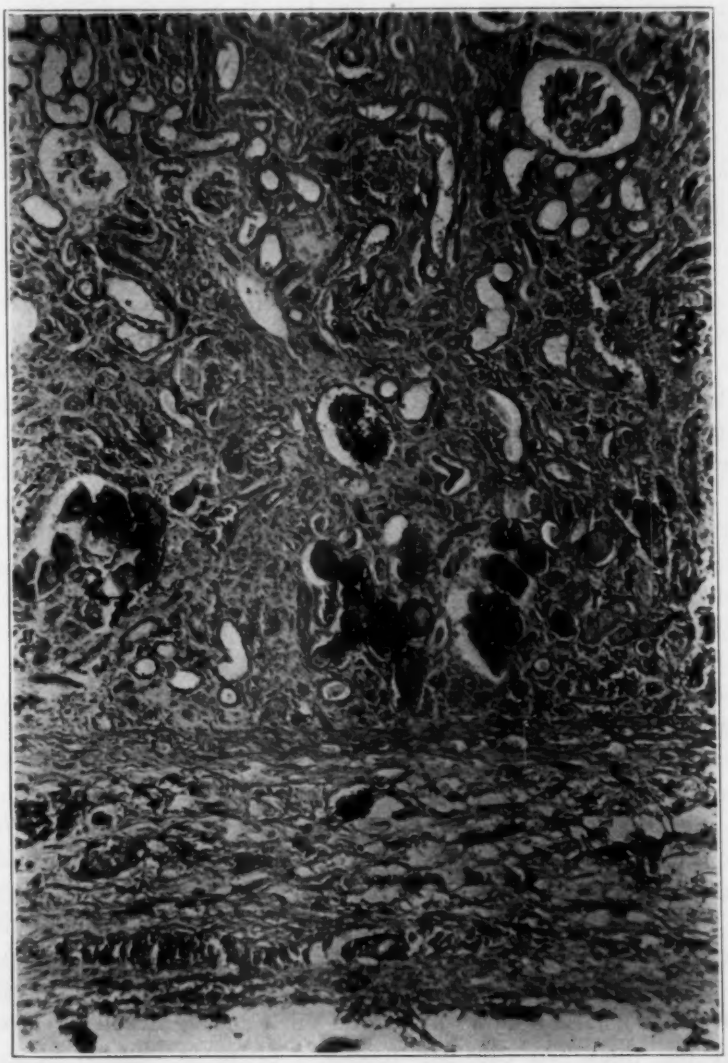

Fig. 9 (experiment 8).—Right kidney eighteen days after formation of a renal arteriovenous fistula. (For gross picture see figure 4.) The dilated capsular and perinephric vessels are well seen. There is diffuse cortical interstitial fibrosis. The various types of tubular change are apparent, and the deposition of calcium within the lumens of necrotic tubules is marked by the deeply stained masses near the capsule.

persistent rise in the pulse rate but no significant elevation of the systolic blood pressure. The animal is alive and well at the time of writing, and a loud bruit can be heard over the right flank.

Experiment 12.—In a male dog weighing 33 pounds (15 Kg.) a right carotid loop was fashioned on April 22, 1938, and between April 26 and May 16 the average daily blood pressure was 90. On May 16 a right renal arteriovenous fistula 1.8 cm. long was made, and a silver wire band was placed around the artery proximal to this. A slight transient rise in blood pressure, pulse rate and the urea nitrogen content of the blood appeared during the first four postoperative days, and on May 20 the silver wire band was constricted until only a slight thrill could be felt over the fistula. The right kidney was then removed. No change in the vital signs has appeared, and the dog is alive and well at the present time. A faint bruit can be heard at one point in the right flank.

COMMENT

Pathology.—The kidney distal to an arteriovenous fistula between its vessels rapidly undergoes a series of changes which culminate in entire replacement of the organ by dense fibrous tissue and calcium. For two to four days after the formation of the fistula the organ is enlarged, deep reddish purple and obviously intensely congested. This impression is corroborated by histologic study, which reveals engorgement of all the smaller vessels with numerous diffuse interstitial hemorrhages. A varying amount of parenchymal damage is evident, but tubular changes are always seen and usually consist in granular swelling of the epithelial cells of all parts, with desquamation of many of the cells of the descending limbs of Henle's loops and of the proximal convoluted tubules.

About six days after the formation of the fistula the kidney becomes pale and begins to decrease in size in spite of the presence of many small collateral vessels which now become evident in the rather thickened perinephric tissues. On section the parenchyma is pale yellow, but the usual markings can be discerned. There is a well defined area of red about the course of the arcuate vessels between the cortex and the medulla (fig. 8). During the earlier part of this period the organ is firm, but as dissolution of the renal elements progresses the tissues become soft, and small granules of gritty material can be felt in the outer cortex. The histologic picture eighteen days after the formation of the fistula (fig. 9) shows numerous small engorged collateral vessels within the thickened capsular tissues. There is diffuse interstitial fibrosis. The tubular changes noted earlier have proceeded either to necrosis of the structure or to one of various stages of reconstruction and healing. Those tubules or parts thereof which die are, when located near the periphery of the cortex, represented by plugs of acidophilic material containing basophilic granules which take the von Kossa stain and appear to be calcium.

Between the twentieth and thirtieth days the kidney undergoes anemic necrosis, which usually involves the entire organ, though a few renal elements about the pelvis and the arcuate vessels and just beneath the capsule may survive for a longer time. The organ is about half the normal size and is embedded in dense, rather vascular fibrous tissue. The parenchyma is pale yellow, and the usual markings are absent. The cortex, the medulla and many of the pyramids are separated by wide bands of pale fibrous tissue and fat (fig. 5). Between these are islands of caseous material containing varying amounts of calcium. A section taken at this time and viewed under the microscope reveals the "ghosts" of the renal structures infiltrated with young fibrous tissue and a few inflammatory cells, most of which are mononuclear. Dilated collateral vessels are no longer so greatly in evidence.

Pathologic Physiology.—In Holman's recent monograph [6] the general circulatory changes known to follow the establishment of an arteriovenous fistula of adequate size have been discussed. Undoubtedly certain of these changes affected the hemodynamics in this series of animals. We did not, however, observe any increase in pulse rate after the formation of one fistula or of bilateral fistulas which could not be attributed to another and more probable cause. Studies of the blood volume and cardiac output were not made. We did not find definite evidence of cardiac hypertrophy. It is probable that our failure to note any of the significant clinical or postmortem signs usually found in the presence of an arteriovenous fistula was due to the small caliber of the openings and the short periods of observation.

The local circulatory changes induced by the formation of a fistula between the renal vessels are similar to those appearing about any physiologically significant [7] communication of this nature. The exact mechanism which stimulates the formation of an extensive collateral blood supply to the structure distal to the short circuit is not completely understood. It is of interest to note that after the kidney is functionally useless the rich anastomotic supply becomes progressively less abundant.

In dogs between 30 and 45 pounds in weight the formation of an arteriovenous fistula greater in length than 9 mm. diverts a part of the renal blood supply sufficient eventually to inhibit completely the excretory utility of the kidney.

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6. Holman, E.: Arteriovenous Aneurysm: Abnormal Communications Between the Arterial and Venous Circulations, New York, The Macmillan Company, 1937.

7. Clark, E. R., and Clark, E. L.: Observations on the Living Preformed Blood Vessels as Seen in a Transparent Chamber Inserted in the Rabbit's Ear, Am. J. Anat. **49**:441, 1932.

If bilateral fistulas of adequate size are established (experiments 2, 5, 7 and 8), or if the normal kidney opposite to that in which a fistula is present is removed (experiment 3, fig. 6), the dog dies in uremia in four to seven days. However, small amounts of dilute urine may be excreted during the early postoperative period, and in experiment 6 it was found that urine containing a diminished amount of urea was excreted as late as eight days after the formation of a fistula between the main vessels of the kidney.

Intravenous pyelograms taken at two, fifteen and thirty-five minutes in experiments 4, 5, 6 and 7 and a differential phenolsulfonphthalein test in experiment 6 demonstrate the inability of the kidney beyond the lesion to excrete either the diodrast or the dye in concentrations equal to those obtained from normal kidneys.

Since, however, the construction of small bilateral fistulas (experiment 1, fig. 4) does not result in fatal uremia, we believe that the chief handicap to renal function in this condition is the lack of circulation of an adequate amount of blood through the organ. This impression is confirmed by the fact that ligation of the renal vein between a large arteriovenous fistula and the vena cava (experiment 7, fig. 7) resulted in a transient fall in an otherwise progressive rise of the level of urea nitrogen in the blood. This effect was presumably due to a temporary increase in the renal blood flow.

The aforementioned changes seem to indicate that a renal arteriovenous fistula renders the involved kidney ischemic. This method of producing ischemia is different from those heretofore reported, and only a mild degree of hypertension is produced (protocols and figs. 4 and 7). Constriction of the renal arteries,[1] ligation of the ureters [8] or compression of the kidneys with ribbon gut [9] results in severe systemic hypertension. Blalock [10] has offered good evidence that the hypertension produced by ligation of the ureters is in reality secondary to renal ischemia. Similarly, it is probable that direct compression of the kidney is effective in causing a rise in arterial tension, because by this means the renal blood flow is diminished. Complete occlusion of the renal arteries in the presence of an adequate collateral circulation is effective in pro-

8. Harrison, T. R.; Mason, M. F.; Resnik, H., and Rainey, J.: Changes in Blood-Pressure in Relation to Experimental Renal Insufficiency, Tr. A. Am. Physicians **51**:280, 1936. Levy, S. E.; Mason, M. F.; Harrison, T. R., and Blalock, A.: The Effects of Ureteral Occlusion on the Blood Flow and Oxygen Consumption of the Kidneys of Unanesthetized Dogs, Surgery **1**:238, 1937.

9. Glenn, F., and Lasher, E. P.: Unpublished data.

10. Levy, S. E.; Light, R. A., and Blalock, A.: The Blood Flow and Oxygen Consumption of the Kidney in Experimental Renal Hypertension, Am. J. Physiol. **122**:38, 1938.

ducing a well sustained increase in tension.[11] One would therefore expect the severe renal ischemia distal to an arteriovenous fistula to be sufficient to produce a similar result.

There is, however, at least one apparent difference between the circulation distal to a Goldblatt clamp and that beyond an arteriovenous fistula. Though in either instance there is a diminution in the arterial pressure, a rise in venous pressure within the renal vein after the application of a Goldblatt clamp to the artery has not been demonstrated. This rise is known to occur distal to an arteriovenous fistula.[12] That the level of venous pressure may be significant is indicated both by these experiments and by studies reported several years ago[13] in which it was found that constriction of the renal vein produced a mild systemic hypertension in no way so great as that which follows partial occlusion of the renal artery.

It is our impression, therefore, that a high venous pressure within the kidney may inhibit significantly the formation or dissemination of the "effective substance" hypothecated by Goldblatt. Recently published experiments by Blalock and Levy[14] would tend to refute this, but sufficient data are not given in their report.

SUMMARY

1. A satisfactory technic for the production of an arteriovenous fistula between the renal vessels of the dog is described.

2. Certain of the pathologic changes observed in and about the kidney distal to such a lesion are pointed out.

3. A few of the physiologic changes appearing subsequent to the formation of this type of fistula are discussed in relation to: (*a*) general circulatory dynamics; (*b*) local circulatory changes; (*c*) kidney function, and (*d*) renal ischemia.

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11. Goldblatt, H.: Studies on Experimental Hypertension: V. The Pathogenesis of Experimental Hypertension Due to Renal Ischemia, Ann. Int. Med. **11**: 69, 1937.

12. Ney, E.: Ueber die Bedeutung der Venen bei arteriovenösen Aneurysmen, Arch. f. klin. Chir. **100**:531, 1912-1913.

13. Bell, E. T., and Pedersen, A. H.: The Causes of Hypertension, Ann. Int. Med. **4**:227, 1930. Pedersen, A. H.: A Method of Producing Experimental Chronic Hypertension in the Rabbit, Arch. Path. **3**:912 (May) 1927. Menendez, E. B.: Stase veinuse du rein normal au énervé et hypertension artérielle, Compt. rend. Soc. de biol. **113**:461, 1933.

14. Levy, S. E., and Blalock, A.: Experimental Attempts to Prevent or Abolish the Hypertension That Is Associated with Renal Ischemia, Surgery **3**: 899, 1938.

PROTOCOLS AND PATHOLOGIC REPORTS

In the following tabulations, A-V signifies arteriovenous; B.U.N., urea nitrogen content of the blood; B.P., blood pressure; P., pulse rate.

PROTOCOL

Experiment 1: Subject, male dog weighing 26½ pounds (12.2 Kg.)

Feb. 19, 1938	Left renal A-V fistula 8 mm. long
Feb. 21	B.U.N. 18.6
March 18	Right carotid loop
March 23–May 5	Average daily B.P. 95 P. 80
May 6	Exploratory laparotomy; fistula patent
May 7–May 20	Average daily B.P. 95 P. 94
May 21	Right renal A-V fistula 9 mm. long
May 22	B.P. 90 P. 80
May 23	B.U.N. 30.7 B.P. 90 P. 108
May 24	B.U.N. 64.7 B.P. 110 P. 100
May 25	B.U.N. 64.3 B.P. 130 P. 116
May 26	B.U.N. 62.9 B.P. 120 P. 92
May 27	B.U.N. 63.8 B.P. 120 P. 92
May 28	B.U.N. 64.3
May 31	B.U.N. 40.5 B.P. 110 P. 84
June 2	B.U.N. 50.7 B.P. 100 P. 96
June 7	B.U.N. 11.0 B.P. 100 P. 96

At the time of writing the animal is still alive, and both fistulas are patent.

PROTOCOL

Experiment 2: Subject, male dog weighing 30 pounds (13.6 Kg.).

Feb. 7, 1938	Right renal A-V fistula 1 cm. long
Feb. 11	Right carotid loop
Feb. 14	B.U.N. 17.0
Feb. 17–Feb. 28	Average daily B.P. 100
Feb. 28	Left renal A-V fistula 1 cm. long
March 1	B.P. 160
March 2	B.U.N. 69.9 B.P. 160
March 3	B.U.N. 139.8 B.P. 145
March 4	B.U.N. 136
March 4	(fourth postoperative day) Dog died with uremia

PATHOLOGIC PICTURE

Gross.—The right kidney was approximately one-third the normal size. It was represented by islets of homogeneous yellow tissue separated by bands of fibrous tissue containing fat. The capsule was extremely adherent. Collateral vessels were rather numerous but were small.

The left kidney was deep reddish purple and slightly larger than normal. The capsule stripped easily, leaving a smooth surface. On section the parenchymal markings were somewhat obscured, owing to the dark color. The peripheral 3 to 4 mm. of the cortex was light yellowish red. A deep red band marked the corticomedullary junction.

Microscopic.—The mass representing the right kidney was composed of granular acidophilic débris containing numerous basophilic granules. Interspersed between these were wide bands of dense fibrous tissue infiltrated with large mononuclear

cells and lymphocytes. The large veins presented greatly thickened walls. The arteries were not remarkable.

Section of the left kidney showed extreme engorgement of all the small vessels, with numerous scattered areas of hemorrhage in both the cortex and the medulla. There was evidence of extensive tubular damage, most marked in the descending loops of Henle and in the proximal convoluted tubules. The glomerular tufts were in most instances bloodless. There were a few red cells in many of the capsules of Bowman.

PROTOCOL

Experiment 3. Subject, a male dog weighing 31 pounds (14 Kg.).

Feb. 18, 1938	Left renal A-V fistula 1 cm. long
Feb. 25	Right carotid loop
March 7	B.U.N. 19.4 B.P. 150
March 7	Right nephrectomy
March 8	B.U.N. 37.2 B.P. 140
March 9	B.U.N. 61.2 B.P. 130
March 10	B.U.N. 119.0 B.P. 170
March 11	B.U.N. 162.3 B.P. 140
March 11	(fourth postoperative day) Dog died with uremia

PATHOLOGIC PICTURE

Gross.—The left kidney was about half the size of the one removed at operation. It was embedded in a thickened capsule containing vessels of a well established collateral circulation. The capsule stripped easily, leaving a smooth surface. On section the parenchyma was pale and its markings somewhat indistinct.

Microscopic.—Section of the left kidney showed engorgement of the small vessels in the cortex, with a few small areas of interstitial hemorrhage. The capillary loops of the glomeruli were poorly filled with blood. The capsules of Bowman were dilated. There was good preservation of the anatomic markings of the tubules in both cortex and medulla.

PROTOCOL

Experiment 4. Subject, male dog weighing 36 pounds (16.3 Kg.).

March 8, 1938	Right carotid loop
March 12-March 19	Average daily B.P. 120
March 19	Right renal A-V fistula 1 cm. long
March 21	B.U.N. 35.9 B.P. 120
March 22	B.U.N. 20.3 B.P. 120
March 23	B.U.N. 16.7 B.P. 100
March 25	B.U.N. 16.2 B.P. 100
March 30	Intravenous pyelogram; visualization on left only
April 6	(eighteenth postoperative day) Dog died of distemper

PATHOLOGIC PICTURE

Gross.—The left kidney was apparently normal. The right kidney was slightly larger than the left. The capsule was thickened and contained numerous dilated vessels. On section the parenchyma was mottled yellow and red. The usual markings were indistinct. The corticomedullary junction was marked by an irregular purple band. The medulla was yellowish white and soft.

Microscopic.—Section of the right kidney showed a picture very similar to that described in the right kidney in experiment 5, though calcium deposition was more plentiful in the present instance. Section of the left kidney showed no significant pathologic changes.

PROTOCOL

Experiment 5. Subject, male dog weighing 41½ pounds (19 Kg.).

March 21, 1938	Right carotid loop
March 26-April 2	Average daily B.P. 110
March 30	Intravenous pyelogram; bilateral visualization
April 2	Right renal A-V fistula 1.2 cm. long
April 4	B.U.N. 16.3 B.P. 120 P. 118
April 11	B.U.N. 18.2 B.P. 110 P. 80
April 20	Left renal A-V fistula 1.8 cm. long
April 21	Intravenous pyelogram; no visualization
April 21	B.U.N. 71.7 B.P. 110 P. 80
April 22	B.U.N. 117.4 B.P. 120 P. 92
April 23	B.U.N. 157.9 B.P. 150 P. 96
April 25	B.U.N. 204.5
April 25 (fifth postoperative day)	Dog died of uremia

PATHOLOGIC PICTURE

Gross.—The left kidney was approximately four times normal size. Its peritoneal surface was lightly adherent to the omentum and to an adjacent loop of small bowel. The parenchyma was deep purplish red. The capsule stripped easily, leaving a smooth friable surface. On section the parenchymal markings were indistinct. There were a few scattered light yellow areas, suggesting early anemic necrosis.

The right kidney was pale yellow and was less than one-half the normal size. The surrounding tissues were thickened and contained numerous dilated anastomotic vessels. On section the parenchyma was yellow throughout, and broad bands of gray fibrous tissue were evident. There were scattered islets of yellowish soft material in the more peripheral part of the organ.

Microscopic.—Section of the right kidney showed the changes of anemic necrosis in almost the entire organ. A few glomerular and tubular elements were preserved about the arcuate vessels and were embedded in dense fibrous tissue. The left kidney presented the changes of early anemic necrosis and infiltration with a few polymorphonuclear and mononuclear leukocytes. There was extensive interstitial hemorrhage, more marked in the medulla.

PROTOCOL

Experiment 6. Subject, male dog weighing 40 pounds (18.1 Kg.).

March 21, 1938	Right carotid loop
March 28-April 8	Average daily B.P. 110
March 30	Intravenous pyelogram; bilateral visualization
April 8	Right renal A-V fistula 2 cm. long
April 9	B.P. 110 P. 132
April 11	B.U.N. 22.4 B.P. 90 P. 140
April 15	Bilateral cutaneous ureterostomies

April 16	Catheters inserted and differential phenolsulfonphthalein test done, showing 10 per cent less excretion of dye on the right in one hour. The right kidney excreted 18 cc. of urine in forty-three minutes and the left 36 cc. That excreted on the right contained 0.820 Gm. of urea nitrogen per liter and that on the left 9.3 Gm.
April 18	B.U.N. 109
April 19	Dog died of bilateral pyelonephritis

PATHOLOGIC PICTURE

Gross.—Both kidneys were almost completely destroyed by infection, the tissue being soft, friable and dark red.

PROTOCOL

Experiment 7. Subject, male dog weighing 46 pounds (20.9 Kg.).

March 22, 1938	Right carotid loop
March 30	Intravenous pyelogram; bilateral visualization
March 31-April 8	Average daily B.P. 100
April 9	Right renal A-V fistula 1.5 cm. long
April 11	B.U.N. 17.3 B.P. 110 P. 100
April 21	Intravenous pyelogram; visualization on left only
April 29	Left renal A-V fistula 7 mm. long
April 30	B.U.N. 49.3 B.P. 160 P. 88
May 2	B.U.N. 127.2 B.P. 120 P. 88
May 3	B.U.N. 159.3 B.P. 130 P. 108
May 4	Ligation renal vein at vena cava; ether anesthesia
May 4	B.U.N. 174.7
May 5	B.U.N. 214.3 B.P. 165 P. 116
May 6	B.U.N. 217.0 B.P. 165 P. 120
May 7	B.U.N. 211.5 B.P. 160 P. 108
May 9	B.U.N. 161.7 B.P. 160 P. 124
May 10	B.U.N. 172.4 B.P. 140 P. 132
May 11	B.U.N. 201.7 B.P. 160 P. 168
May 12	B.U.N. 252.4 B.P. 120 P. 176
May 12 (thirteenth postoperative day)	Dog died of uremia

PATHOLOGIC PICTURE

Gross.—The left kidney was deep purple but approximately normal in size. The perirenal tissues were slightly indurated and contained a few small areas of diffuse hemorrhage. The capsule stripped easily, leaving a smooth surface. Several dilated collateral capsular vessels were present. On section the parenchyma presented no striking changes except those of congestion.

The right kidney was slightly smaller than normal and was embedded in thickened fibrous tissue containing an abundant collateral circulation. In a few places the capsule was adherent to the parenchyma by delicate strands of fibrous tissue. On section the anatomic markings were present but indistinct. The medulla was bright yellow, as was an arc of tissue in the region of the arcuate vessels. The cortex was pinkish yellow and presented punctate areas which were lighter in color and contained particles of gritty material.

Microscopic.—Section of the left kidney showed changes very similar to those described for the right kidney in experiment 8. There was evidence, however, of more advanced tubular degeneration and of more extensive deposition of calcium.

PROTOCOL

Experiment 8. Subject, male dog weighing 42 pounds (19.1 Kg.).

March 21, 1938	Right carotid loop
April 7-April 25	Average daily B.P. 110
April 21	Intravenous pyelogram; bilateral visualization
April 24	Right renal A-V fistula 1.2 cm. long
April 26	B.P. 120 P. 108
April 27	B.P. 160 P. 104
April 28	B.U.N. 19.9 B.P. 160 P. 80
May 6	Left renal A-V fistula 8 mm. long
May 7	B.U.N. 41.0 B.P. 170 P. 72
May 9	B.U.N. 143.0 B.P. 140 P. 100
May 10	B.U.N. 152.3 B.P. 160 P. 100
May 11	B.U.N. 214.3 B.P. 200 P. 88
May 12	B.U.N. 266.4 B.P. 205 P. 100
May 13	(seventh postoperative day) Dog died of uremic convulsion

PATHOLOGIC PICTURE

Gross.—The left kidney was surrounded by a large area of ecchymosis. Collateral vessels were not evident. The capsular surface was smooth, and on section the parenchyma was deep purplish red. Immediately beneath the capsule were a few tiny areas of light yellow discoloration. The right kidney (fig. 4) was approximately one-half the normal size. The perirenal tissues were thickened and contained numerous dilated collaterals. The capsule stripped easily. On section the parenchyma was light pinkish yellow, and normal cortical markings could be discerned. The medulla, however, was uniformly light yellow. In the more peripheral part of the cortex were small areas of soft yellow material containing granules suggestive of calcium.

PROTOCOL

Experiment 9. Subject, male dog weighing 31½ pounds (14.2 Kg.).

March 25, 1938	Right carotid loop
March 31-April 9	Average daily B.P. 90
April 29	Right renal A-V fistula 1 cm. long
April 30	B.P. 90 P. 96
May 2	B.U.N. 14.9 B.P. 140 P. 92
May 3	B.P. 160 P. 84
May 4	B.P. 120 P. 84
May 5	B.P. 120 P. 76
May 6	B.P. 110 P. 76
May 9-June 15	Average daily B.P. 100 P. 72
June 16	Animal killed

PATHOLOGIC PICTURE

Gross.—The left kidney was apparently normal. The right kidney was about one-half the size of the left, and the capsule about the hilus was thickened with scar tissue. On section the parenchyma was not remarkable except for a slight increase in fibrous tissue about the arcuate vessels and between the medullary pyramids. The site of the vascular anastomosis presented a tiny ring of scar

completely plugged by a mass of pale, partially organized fibrin which projected 1 to 2 mm. into the lumen of the vein. Neither the artery nor the vein was occluded.

PROTOCOL

Experiment 10. Subject, male dog weighing 41 pounds (18.6 Kg.).

May 14, 1938	Right carotid loop
May 19-June 2	Average daily B.P. 100 P. 72
June 2	Right renal A-V fistula 11 mm. long
June 3	B.P. 100 P. 92
June 4-June 15	Average daily B.P. 110 P. 92
June 16 (fourteenth postoperative day)	Dog killed for injection of vessels with Hill's solution

PATHOLOGIC PICTURE

Gross.—The left kidney was apparently normal. The right kidney was soft, light pinkish yellow and slightly larger than the left. On section the parenchymal markings were indistinct, and the entire structure resembled somewhat that of the right kidney in experiment 8 (fig. 4).

PROTOCOLS

Experiment 11. Subject, male dog weighing 37½ pounds (17 Kg.).

April 22, 1938	Right carotid loop
April 29-May 20	Average daily B.P. 120 P. 70
May 24	Right renal A-V fistula 1 cm. long
May 25	B.P. 130 P. 100
May 31	B.P. 120 P. 92
June 1-June 16	Average daily B.P. 120 P. 100 Animal alive and well; loud bruit present

Experiment 12. Subject, male dog weighing 33 pounds (15 Kg.).

April 22, 1938	Right carotid loop
April 26-May 16	Average daily B.P. 90
May 16	Right renal A-V fistula 1.8 cm. long Silver wire band placed around renal artery proximal to fistula
May 17	B.U.N. 21.4 B.P. 120 P. 84
May 18	B.P. 100 P. 112
May 19	B.P. 120 P. 124
May 20	B.U.N. 19.5
May 20	Exploratory laparotomy; silver wire band on renal artery tightened to constrict vessel so that only a slight thrill could be felt; right nephrectomy
May 21-June 16	Average daily B.P. 110 P. 104 Animal alive and well; bruit audible

PATHOLOGIC PICTURE

Gross.—The right kidney was deep reddish purple and slightly larger than normal. The capsule stripped easily, leaving a smooth surface. On section the parenchymal markings were fairly distinct, and the general appearance was that of moderate passive congestion of the organ.

REGENERATION OF NERVES AFTER ANASTOMOSIS OF SMALL PROXIMAL TO LARGER PERIPHERAL NERVES

AN EXPERIMENTAL STUDY CONCERNED WITH RELIEF OF PERIPHERAL NEUROGENIC PARESIS

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Recently, Dogliotti [1] recommended and attempted clinically to obtain increased innervation and function in paretic muscles supplied by a partially paralyzed nerve by means of simple section and immediate anastomosis of the involved nerve trunk. He had found experimentally that by anastomosing a portion of the proximal segment to the whole distal segment of the sciatic nerve in the dog he could demonstrate an increase in the number of nerve fibers regenerating below the point of anastomosis. This, in addition to the fact that his animals made a good functional recovery, led him to interpret his results as indicating reinnervation of muscles and a return of muscular function in excess of that originally and normally mediated by the proximal nerve fibers. If this interpretation of Dogliotti's findings is correct and if this procedure should prove practical, its value becomes obvious in the rehabilitation of patients with peripheral neurogenic paresis, such as occurs in cases of anterior poliomyelitis.

Kilvington [2] reported 4 experiments on dogs, involving in 2 instances the anastomosis of the internal popliteal nerve to the peripheral segments of both the internal and the external popliteal nerves. In the other 2 dogs the external popliteal nerve was anastomosed to the external and internal popliteal nerves. Good functional recoveries were observed

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1. Dogliotti, A. M.: Etudes expérimentales et première application clinique d'une nouvelle opération destinée à augmenter et à équilibrer la fonction neuro-musculaire dans la paralysis partielle des nerfs, J. de chir. **45**:30-48, 1935.

2. Kilvington, B.: An Investigation on the Regeneration of Nerves, with a View to the Surgical Treatment of Certain Paralyses, Brit. M. J. **1**:935-940, 1905.

in all but 1 of the animals. After recovery, electrical stimulation above the anastomosis produced contraction of both flexor and extensor muscles. Counts of the nerve fibers in proximal and distal segments of the nerves of 3 of the animals showed an increase in regenerating nerve fibers of 125, 49 and 25.4 per cent.

Kennedy [3] expressed the belief that Kilvington's results could be better evaluated by the use of the forelimb than of the hindlimb. In 2 dogs he anastomosed the proximal segments of the musculocutaneous, median and ulnar nerves (flexors) to their peripheral segments and to the musculospiral nerve. In 3 other dogs the musculospiral nerve alone (extensor) was anastomosed to the combined peripheral segments of the musculocutaneous, median, ulnar and musculospiral nerves. In the animals showing recovery, electrical stimulation of the central segments produced contractions of both flexor and extensor muscles. The same was found to be true on stimulation of the corresponding cortical centers, while stimulation of the centers associated with nerves eliminated from the anastomoses gave no response. Counts of the nerve fibers were not made.

Feiss [4] attempted anastomosis of a single proximal nerve to two peripheral nerves by what he termed a process of "fusion." This consisted of ligating the peripheral segment of one nerve to the side of another nerve with catgut after both nerves had been crushed at the point of ligation. By this method he was able to demonstrate successful regeneration from one proximal nerve to two peripheral nerves. As would be expected, the regeneration through the neuroma which formed at the site of ligature was limited, being considerably less than that which might be expected after proper end to end anastomosis of nerves. Application of this method to a human patient suffering from the paresis of poliomyelitis was attempted by Feiss,[5] without convincing results.

Anastomoses of the proximal portion of one nerve to the peripheral portions of two or more nerves in human patients, with varying degrees of success, have been reported by numerous authors. Most of these have been clinical attempts to overcome severe palsy of the facial nerve

3. Kennedy, R.: Experiments on the Restoration of Paralyzed Muscles by Means of Nerve Anastomosis: II. Anastomosis of the Nerve Supplying Limb Muscles, Phil. Tr. Roy. Soc., London, s.B **205**:27-76, 1914; abstracted, Proc. Roy. Soc., London, s.B **87**:331-335, 1914.

4. Feiss, H. O.: On the Fusion of Nerves, Quart. J. Exper. Physiol. **5**:1-30, 1912.

5. Feiss, H. O.: Recent Experimental Work on the "Fusion" of Nerves and Its Practical Bearing on Infantile Paralysis: Report of a Case of Infantile Paralysis Treated by This Method, Boston M. & S. J. **164**:667-671, 1911.

and have involved the anastomosis of the spinal accessory or the hypoglossal nerve to the facial nerve. These procedures did not involve the reinnervation of antagonistic muscles. Control studies to determine the degree of reinnervation of nerve and muscle were, of course, impossible.

Observations on the increased number of regenerating nerve fibers below the point of an anastomosis have also been made by Greenman [6] 1913, Ballerini [7] 1923, Milone [8] 1924, Nageotte [9] 1932, Purpura [10] 1930 and others. The phenomenon of luxuriant regeneration of nerves, however, is not adequate evidence for the conclusion that function is equally enhanced. An analysis of the problem reveals that certain control studies are necessary before final acceptance of such a point of view.

In the first place, it is essential to determine whether fewer, the same number or more nerve fibers regenerate after simple section and immediate anastomosis of a whole nerve trunk. Under such conditions an increased number of regenerating fibers can scarcely be interpreted as evidence for an increased innervation of muscle fibers, since presumably the original number of nerve fibers was physiologically adequate for complete innervation of all the muscles supplied by the nerve in question. Would it then follow that under the conditions described by Kilvington, Purpura, Dogliotti and others an increased number of regenerating nerve fibers necessarily implies an increased final innervation and function of the muscles supplied? In this connection Nageotte [9] wrote:

> It is important to note that the number of regenerating fibers in the lower stump does not correspond with that of the afferent fibers which have traversed the cicatrix. In a lacerated wound, one may see the inferior stump of the divided nerve receive only a few neurites and nevertheless contain an almost normal number of fibers; here anatomical regeneration is good, but physiological regeneration is poor.

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6. Greenman, M. J.: Studies on the Regeneration of the Peroneal Nerve of the Albino Rat: Number and Sectional Areas of Fibers; Area Relation of Axis to Sheath, J. Comp. Neurol. **23**:479-513, 1913.

7. Ballerini, M.: Sul rapporto fra il numero delle fibre rigenerate e quelle preesistenti in un nervo interrotto con la strozzatura, Gior. d. r. Accad. di med. di Torino **29**:150-157, 1923.

8. Milone, S.: Ricerche sulle consequenze dell'unione di un moncone nervoso centrale di piccolo calibro con un moncone periferico di grosso calibro, Gior. d. r. Accad. di med. di Torino **30**:50-53, 1924; Arch. per le sc. med. **47**:107-124, 1924.

9. Nageotte, J.: Sheaths of the Peripheral Nerves: Nerve Degeneration and Regeneration, in Penfield, W.: Cytology and Cellular Pathology of the Nervous System, New York, Paul B. Hoeber, Inc., 1932, vol. 1, sect. 5, pp. 215-231.

10. Purpura, F.: Distribuzione delle fibre nei trorchi nervosi e chirurgia dei nervi periferici, Policlinico (sez. chir.) **38**:643-652, 1931.

Secondly, it would seem essential to have control studies under conditions corresponding to those obtaining in a case of peripheral neurogenic muscular paresis. Delay in regeneration of the nerve and the fibrotic changes in nerve and muscle which follow degeneration under these conditions might result in a less satisfactory regeneration of nerve and muscle and less complete functional recovery than that found after immediate anastomoses, such as those performed by Purpura,[10] Dogliotti,[1] Gaglio and Parrinello[11] and Iovino.[12] These conditions could be approximated experimentally by delaying for a considerable period the anastomosis of the central nerve stump to a larger peripheral nerve (Kilvington procedure), the peripheral nerve having been partially paralyzed by previous section of the central stump. Furthermore, to evaluate properly this factor of delay it would be necessary to repeat the Kilvington procedure, using the same nerves and the same technic but accomplishing the anastomosis without delay.

Thirdly, the important question of whether good functional reinnervation may be obtained in one group of muscles by the use (Kilvington procedure) of nerves supplying antagonistic muscles seemed to merit further demonstration and study, particularly in connection with the control studies proposed.

With such questions in mind and to determine the practicability of this procedure the present work was undertaken.

METHODS

Operative Procedure.—Under aseptic conditions the right sciatic nerve in 4 dogs was exposed by a posterior approach in the lower portion of the thigh and the popliteal space. The common peroneal and tibial nerves were isolated, and identification was checked by the muscular response elicited by faradic stimulation of the individual nerves. Both nerves were carefully sectioned at the same level with a sharp scalpel. In 2 dogs an immediate anastomosis was performed between the proximal end of the common peroneal nerve and the distal ends of the common peroneal and tibial nerves combined. In these 2 dogs the proximal end of the tibial nerve was doubly ligated with heavy corded silk and was sutured to one side in neighboring muscles. This served (1) to check the results of Kilvington, Dogliotti and others, (2) to test the feasibility of obtaining satisfactory recovery of antagonistic muscle groups by the use of the nerve normally supplying one group only and (3) as a standard of comparison for the control experiment on 1 of the 2 remaining animals, in which the anastomosis was performed later to approximate the usual clinical conditions of prolonged partial paralysis. As a control under prolonged conditions of partial paralysis (see introductory section),

11. Gaglio, V., and Parrinello, J.: Sulla fasciolazione e sulla sistematizzazione delle fibre nervose del radiale a dell'ulnare del cane, nel tratto omerale, Arch. ital. di anat. e istol. pat. **4**:731-750, 1933.

12. Iovino, F.: Sull'aumento numerico delle fibre dei nervi in rigenerazione, Chir. d. org. di movimento **21**:193-199, 1936.

in 1 dog the common peroneal nerve alone was cut and both ends were ligated with corded silk. One month later this dog was operated on again through a fresh incision. The ligated nerves were found, and the ends were dissected free and resected to eliminate all cicatricial tissue produced by the ligatures. The tibial nerve was next sectioned at the same level. The proximal stump of the common peroneal nerve was then anastomosed to the distal ends of the common peroneal and the tibial nerve combined. The proximal stump of the tibial nerve was ligated twice with heavy corded silk and sutured to one side in neighboring muscles.

In the fourth dog, also a control (see introductory section), the common peroneal and the tibial nerves were cut, and immediate anastomosis was performed between the proximal and distal ends of each.

In all cases end to end anastomoses were performed, three or four fine arterial silk sutures being used in the sheaths of the nerves.

Follow-up Studies.—Repeated examinations were made of all the animals, the follow-up period varying from seven to nine and one-half months. Finally, in each case the operative site was again exposed with the animal under light ether anesthesia. The operative area was examined; the condition of the anastomosis was determined, and the absence of complicating fibers from the tibial or other neighboring nerves was verified. The effects of faradic stimulation of the sciatic nerve above the anastomosis were noted, as were the effects of such stimulation of the common peroneal and the tibial nerve individually below the anastomosis.

Pathologic Preparations.—Specimens were next dissected out with care from the following points: the right sciatic nerve, the right common peroneal nerve above the anastomosis, the right common peroneal nerve and the right tibial nerve below the anastomosis. Likewise, the entire gastrocnemius and tibialis anticus muscles were dissected out on both the right and the left side in each case. The muscles were weighed, and specimens were taken from each for pathologic study. The specimens both of nerves and muscles were fixed in Zenker's solution. Cross sectional cuts of the nerves were made from paraffin blocks. These were mounted, overstained with hematoxylin and eosin, washed and counterstained with a 2 per cent effusion of crocus (Spanish saffron), according to a technic developed by Mr. William Hewitt, of the department of pathology of the University of California. Routine hematoxylin and eosin stains were done on the specimens of muscle.

Nerve Fiber Counts.—Counts of the nerve fibers, were made with the use of a microscopic carbon arc projector. Cross sectional slides of the nerve trunks were projected and magnified on a large sheet of drawing paper. The ability to focus and determine details of color insured identification of the nerve fibers in all parts of the nerve trunk just as though the section were being studied by the usual technic under the microscope. In these respects the method proved far superior to that of counting from photomicrographic enlargements, being more direct, simple and accurate. The magnification obtained by means of the carbon arc projector is comparable to that obtained in photomicrographic enlargements, and the apparatus may be adjusted readily to whatever magnification is most satisfactroy. The accuracy and ease of counting were materially aided by blocking off in pencil on drawing paper each nerve fiber as it was counted. This projection method possesses the advantages of a microscopic study for focusing and for differentiation of color, and the result has the advantages of the enlarged photomicrograph without the faults and difficulties of production of the latter.

RESULTS

The follow-up findings, weights of the muscles and nerve fiber counts for the 4 dogs studied are presented in table 1.

TABLE 1.—*Results of Anastomosis*

	Dog 39	Dog 93	Dog 34	Dog 499
Weight	15.3 Kg.	17.0 Kg.	26.0 Kg.	19.5 Kg.
Anastomosis	Control—right common peroneal to right common peroneal	Control—right common peroneal ligated; 1 mo. later anastomosed to right sciatic	Right common peroneal to right common peroneal and tibial	Right common peroneal to right common peroneal and tibial
Follow-up studies				
Posture	Normal	Right hock slightly down	Right hock down moderately	Normal
Gait	Normal	Minimal limp	Awkward; often walking on dorsum of right hindpaw	Slight awkwardness
Weakness				
Flexors	None	None	Slight	Slight
Extensors	? Slight	Slight	Moderate	Slight
Muscle atrophy				
Flexors	None	None	Moderate	Moderate
Extensors	? None	Moderate	Moderate	Moderate
Time and degree of motor recovery	Complete in 7 mo.	80-90% in 9½ mo.	60-70% in 7 mo.	70-80% in 7 mo.
Trophic ulcers	None	None	3 sores; no ulcers	None
Hypesthesia	? Slight	Slight	Moderate	? Slight
Time and degree of sensory recovery	? Slight hypesthesia for 8½ mo.	Slight hypesthesia persisting for 9½ mo.	Moderate hypesthesia persisting for 7 mo.	? Slight hypesthesia persisting for 7 mo.
Muscle weight and estimated size of muscle fibers (1 = normal)				
Gastrocnemius muscle				
Right	66.4 Gm.*	74.2 Gm.*	70.5 Gm.	48.5 Gm.
	1.15	1.3	1.37	1.3
Left	61.8 Gm.	72.0 Gm.	103.5 Gm.	85 Gm.
	1	1	1	1
Tibialis anticus muscle				
Right	20.3 Gm.	15.4 Gm.	15 Gm.	15 Gm.
	1.15	1.3	1.37	1.3
Left	25.8 Gm.	26 Gm.	31 Gm.	32.5 Gm.
	1	1	1	1
Nerve fiber counts				
Right sciatic	18,016	13,260	23,950	17,820
Right common peroneal (above anastomosis)	5,504	5,026	7,956	7,088
Right common peroneal and tibial (below anastomosis)	7,474 (common peroneal only)	7,557	15,088	12,533
Increase in nerve fibers	35.7%	50%	90%	76.8%

* This weight is increased over that of its control. This is of interest in relation to the hypertrophy of the muscle fibers in these muscles but may also represent the limits of error of the method in spite of careful dissection and efforts to control the effects of dehydration.

COMMENT

It is interesting to compare the results obtained in dogs 34 and 499 with those reported by other workers using essentially the same procedure but different technics. The latter are presented in table 2 and are in essential agreement with the results obtained in this study.

Do these results necessarily reflect an increased final innervation and function of muscles? As has been mentioned, the increase in the number of nerve fibers may merely reflect a well known phenomenon concerned with the regeneration of nerves and, as pointed out by Nageotte,[9] may bear no relation to the final reinnervation of muscles.

TABLE 2.—*Comparative Results Obtained by Other Authors with Different Technics*

Author	Kilvington[2]			Milone[5]	Dogliotti[1]		Iovino[12]		
Case	2	3	4	..	1	2	1	2	3
Weight	..	..	..	..	..	..	10.5 Kg.	8 Kg.	9 Kg.
Nerve fiber counts									
Sciatic	.....	.....	.....	.....	22,350	16,274	15,096	12,472	12,831
Portion of nerve above anastomosis	4,435	7,740	5,826	2,282	7,200	6,790	6,507	4,945	4,530
Portion of nerve below anastomosis	9,982	9,706	8,688	5,131	14,090	10,555	11,075	9,417	9,913
Percentage increase in nerve fibers	125	25.4	49	123	95	55	70	90	118
Weight of muscles									
Untreated side	.....	.....	.....	.....	72 Gm.	83 Gm.	41.3 Gm.	23.1 Gm.	32 Gm.
Treated side	.....	.....	.....	.....	70 Gm.	81 Gm.	39.5 Gm.	22.75 Gm.	31.5 Gm.
Estimated increase in size of muscle fibers	.....	.....	.....	.....	33%	33%	Larger	Larger	Larger
Degree and time of functional recovery	Incomplete, 3⅗ mo.	Complete, 3½ mo.	Incomplete, 4⅗ mo.		Complete, 7 mo.	Complete, 14 mo.	Complete, 7 mo.	Complete, 8 mo.	Complete, 10 mo.

Evidence has been adduced from two different angles in answer to this question:

1. The results obtained in the control experiment (dog 39) indicate that Nageotte's opinion is justified, at least to a considerable extent. In this instance simple anastomosis of a nerve trunk resulted eight and a half months later in an increase of more than one third in the number of nerve fibers. Yet complete reinnervation of the muscle presumably required only the original number of fibers. The possibility exists that under the conditions of the experiments (i. e., for the reinnervation and regeneration of muscle fibers) more nerve fibers are actually needed and serve a useful physiologic purpose. If this is the case, the same argument holds for the experiments in which Kilvington's procedure was utilized—more nerve fibers are necessary for the same degree of muscu-

lar function. If this is true, an increased number of nerve fibers would not necessarily mean an increased degree of muscular function. Therefore, regardless of the exact interpretation, the results suggest that the phenomenon of luxuriant regeneration of nerves does not bear a direct quantitative relation to reinnervation of muscles and final return of muscular function.

2. A study of the muscles reinnervated after the Kilvington procedure reveals further evidence bearing on this same question. As may be seen from tables 1 and 2, the weight of muscles on the side operated on was appreciably lower in both instances (dogs 34 and 499) than on the opposite side, used as a control. Likewise, it is to be noted that the muscle fibers on the side operated on were uniformly larger than those on the side not operated on. Volume for volume, therefore, the

TABLE 3.—*Estimated Number of Muscle Fibers Successfully Reinnervated*

	Dog 34		Dog 499	
	Gastrocnemius	Tibialis Anticus	Gastrocnemius	Tibialis Anticus
Weight of muscles				
Untreated side	103.5 Gm.	31 Gm.	85 Gm.	32.5 Gm.
Treated side	70.5 Gm.	15 Gm.	48.5 Gm.	15 Gm.
Estimated size of muscle fibers (normal = 1)				
Untreated side	1	1	1	1
Treated side	1.37	1.37	1.3	1.3
Estimated percentage of fibers in muscles on treated side (percentage of fibers on untreated side = 100)	50	35	44	35

fibers on the side operated on must be fewer. This fact, combined with the over-all diminution in size of the muscle on the side operated on, as measured by the respective weight of each, yields interesting estimates (table 3), on a percentage basis, of the number of fibers in muscles on the side operated on as compared with their respective controls (100 per cent) on the normal side.

By the Kilvington procedure as used in this study, however, the common peroneal nerve alone supplied the nerve fibers for both extensor and flexor muscles. The number of fibers in this nerve is roughly 30 per cent or more of the number present in the sciatic nerve. Also, the estimated number of regenerating muscle fibers in the extensor muscles on the side operated on, as judged from the tibialis anticus muscle, is 35 per cent, while the flexor muscles on the side operated on are estimated to have approximately 44 to 50 per cent of their normal number of muscle fibers.

Since the flexor muscles are more than twice the size of the extensor muscles it may be safely estimated that the number of successfully reinnervated muscle fibers after the Kilvington procedure as performed in

this study is at least 10 per cent greater than the original number of extensor muscle fibers normally innervated by the common peroneal nerve. This is shown diagrammatically in the accompanying illustration.

This evidence tends to support Dogliotti's contention. It is to be noted, however, that in these two experiments the increase in the numbers of regenerating nerve fibers was 76.8 and 80 per cent. These figures are markedly out of proportion to the number of muscle fibers estimated to have been successfully reinnervated. Also, since the follow-up observations (table 1) are in harmony with the findings for the muscles, it may be concluded that regeneration of the nerves was also out of proportion to the return of muscular function.

Even though reinnervation and return of function of the muscles are not in proportion to the regeneration of the nerves after the Kilving-

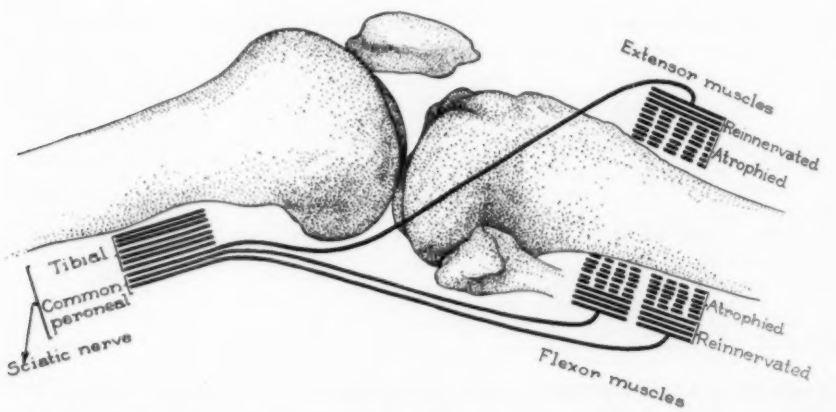

Diagram illustrating the estimated reinnervation of muscles after anastomosis of the proximal end of the common peroneal nerve to the peripheral ends of the tibial and the common peroneal nerve combined. The sciatic nerve fibers are represented by ten lines; the extensor muscle fibers are represented by ten lines, and the flexor muscle fibers are proportionately represented by twenty lines. The broken lines indicate (relatively) the estimated number of muscle fibers not successfully reinnervated. It should be noted that the total number of unbroken "muscle lines" is eleven, while the relative number of "extensor muscle lines," representing muscle fibers normally innervated by the common peroneal nerve, is ten.

ton procedure, the important fact remains that it may be possible by this method to obtain reinnervation and functional recovery of the paretic muscles when the paresis is on a peripheral neurogenic basis.

If a partially paralyzed nerve is severed and immediately anastomosed, an increase of muscular reinnervation and function may reasonably be expected. If a neighboring intact nerve is selected for the anastomosis in the case of a completely or almost completely paralyzed

nerve, there results a diminution in the strength and function of the muscles normally innervated by the intact nerve, considerable recovery in the muscles innervated by the paralyzed nerve and an over-all increase in the number of muscle fibers innervated by the intact nerve. Although the return of strength and function may not be so great as Dogliotti estimated, it is still possible that the procedure may be of practical advantage in properly selected cases. The good results obtained in the control experiment (dog 93) tend to support this idea. In this instance an attempt was made to simulate the condition mentioned by ligating the common peroneal nerve and producing paralysis of the extensor muscles of the right hindleg. One month later the Kilvington procedure was carried out in the same manner as for dogs 34 and 499. In spite of the previous damage to nerves and muscles and an increase of only 50 per cent in the regeneration of the nerves anastomosed to the common peroneal nerve, good reinnervation of the muscle and return of function occurred.

The possibility of good functional reinnervation of two synergistic groups of muscles by the nerve supplying one of these muscle groups, as demonstrated by Kilvington,[2] by Kennedy [3] and by this study, is also of great significance from the standpoint of the practicability of this procedure. If an extensor muscle of the foot, for example, were paralyzed, a fair functional result might reasonably be expected to follow section of one of the branches from the tibial nerve to the gastrocnemius or the soleus muscle and its anastomosis to the distal ends of both the same branch and the common peroneal nerve. Although such an instance might offer a promising opportunity for employment of the Kilvington procedure, it is possible that other conditions might not be so favorable. In the proper selection of cases the following limiting factors should be mentioned:

(*a*) If an intact nerve is selected for the anastomosis the procedure will result in permanent weakening of the muscles previously and normally supplied by that nerve. Hence, only nerves or branches of nerves the loss or partial loss of which will not cause appreciable weakness or loss of function should be selected. Without proper care in this respect the procedure may conceivably result in as much paralysis as that which it is proposed to cure, or more. Indeed, the use of an intact nerve for this procedure does not yet appear to be justified. Because the estimation of functional recovery is so difficult with animals and conclusions based on experimental work frequently require modification when applied to human conditions, any recommendation in this regard (i. e., the use of intact nerves) must be deferred until further data are available on the degree of functional recovery following this procedure (i. e., the use of a partially paralyzed nerve) in man.

(*b*) Reinnervation and recovery of the extensor muscles of the leg are considerably poorer than reinnervation and recovery of the flexor muscles, as shown by the work of Kilvington,[2] that of Dogliotti [1] and the present study. In our experience this was true even though the nerve to the extensor muscles (common peroneal) was selected for the anastomosis (table 1). Thus, in this procedure, the use of the intact common peroneal nerve or its branches should be avoided as far as possible.

(*c*) As has been determined by another experimental study now in progress, an important limiting factor in functional recovery is probably fibrosis of the muscle fibers. Since muscular fibrosis progresses with continued paresis, intervention should take place reasonably early.

CONCLUSIONS

1. Sectioning of the sciatic nerve and immediate anastomosis of the proximal portion of the common peroneal to the peripheral ends of both the common peroneal and the tibial nerve resulted under experimental conditions in a marked increase in the number of regenerating nerve fibers below the point of anastomosis.

2. Reinnervation of muscles and recovery of function following this procedure were increased over the innervation and function originally mediated by the common peroneal nerve alone but under the conditions of this study were not proportional to the luxuriant regeneration of the nerve.

3. Synergistic groups of muscles may be reinnervated successfully and good functional recovery obtained by anastomosis of a nerve supplying one of these muscles to the peripheral portions of the nerves innervating both the groups of synergistic muscles. The flexor muscles of the leg showed recovery considerably better than that of the extensor muscles, even though the common peroneal nerve was selected for the anastomosis.

4. In properly selected cases the sectioning and immediate anastomosis of a partially paralyzed nerve (as, for example, the common peroneal nerve with marked paresis involving the tibialis anticus and the extensor digitorum longus muscle) may prove of practical advantage for treating the isolated paresis occurring in association with poliomyelitis and other peripheral neurogenic paralyses.

FIBROCYSTIC DISEASE OF THE BREAST

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The diversity of terms applied to proliferative and cystic changes in the breast since the recognition of such changes over a century ago illustrates the efforts made to interpret the varied clinical, pathologic and anatomic findings.

The condition was first described by Cooper [1] in 1829, in the chapters on "hydatid," "irritable" and "chronic" mammary tumor in his "Illustrations of the Diseases of the Breast." Included in the early nomenclature are such terms as "abnormal involution of the breast," [2] "cystic disease of the breast (Reclus' disease)," [3] "sero-cystic tumors of the breast," [4] "chronic cystic mastitis," [5] "chronic cystic mastopathia," [6] "cystadenoma (Schimmelbusch's disease)" [7] and "senile parenchymatous hypertrophy." [8a] Later, Bloodgood wrote of "shotty breast" and "blue-domed cyst." [8b] Cheatle and Cutler [9] added "mazoplasia" and "cystiphorous desquamative hyperplasia"—conditions of the breast which, they concluded, differ biologically and morphologically from one another and which together represent the condition generally included in the

1. Cooper, A.: Illustrations of the Diseases of the Breast, London, Longman, Rees & Co., 1829, pt. 1.

2. Warren, J. C.: Surgical Observations on Tumors, with Cases and Operations, Boston, Crocker & Brewster, 1837.

3. Reclus, P.: La maladie kystique des mamelles, Bull. Soc. anat. de Paris **58**:428, 1883.

4. Brodie, B. C.: Clinical Lectures in Surgery, Philadelphia, Lea & Blanchard, 1846, p. 206.

5. König, F.: Mastitis chronica cystica (interstitielle Mastitis, Cystadenoma mammae, Maladie de Reclus), Centralbl. f. Chir. **20**:49 (Jan. 21) 1893.

6. Aschoff, L.: E giustificata l'ammissione di uno stadio preblastomatoso e precanceroso? Tumori **10**:337 (July-Oct.) 1936.

7. Schimmelbusch, C.: Das Cystadenom der Mammae, Arch. f. klin. Chir. **44**:117, 1892.

8. Bloodgood, J. C.: (*a*) Senile Parenchymatous Hypertrophy of the Female Breast: Its Relation to Cyst Formation and Carcinoma, Surg., Gynec. & Obst. **3**:721 (Dec.) 1906; (*b*) Pathology of Chronic Cystic Mastitis of the Female Breast, with Special Consideration of the Blue-Domed Cyst, Arch. Surg. **3**:445 (Nov.) 1921.

9. Cheatle, G. L., and Cutler, M.: Tumors of the Breast, London, Edward Arnold & Co., 1931.

one term "chronic mastitis" or "chronic cystic mastitis." Others [10] subsequently suggested "cystoplasia" as an abbreviation of "cystiphorous desquamative hyperplasia." The condition has also been designated "fibrocystic mastitis" at the New York Post-Graduate Medical School and Hospital.[11] Lewis and Geschickter,[12] on the other hand, used the term "chronic cystic mastitis" to cover the entire condition but recognized two different types, to which they applied the names "cystic disease of the breast" and "adenosis of the breast." "Mastopathia" was regarded by Whitehouse [13] as an appropriate term for the entire picture, in which he included mammary pain and swelling, oligomenorrhea and menstrual headache. Taylor [14] suggested "adenofibrosis," which, he stated, is in harmony with the nomenclature employed for pathologic conditions of the reproductive tract and is similar to the term "fibroadenomatosis cystica mammae," which was adopted by Semb [15] after exhaustive histologic studies.

While it is realized that the condition under discussion is already overburdened with diversified names, it is in the hope of diminishing rather than of adding to the confusion that another title is herewith suggested. The term "fibrocystic disease of the breast" has been chosen because it seems definitely to characterize the outstanding features of the condition, namely, the fibrous and cystic elements. The classification on which this is based is similar to that of Lewis and Geschickter.[12a] The classification here presented, however, recognizes three types of the disease instead of only two. They are: (1) the predominantly cystic type (which includes "Schimmelbusch's disease" and "blue-domed cyst"); (2) the type in which the fibrous element predominates ("adenomatosis," or "shotty breast"), and (3) the type in which both fibrous and cystic elements are present in approximately equal proportions.

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10. Ritvo, M.; Butler, P. F., and O'Neil, E. E.: Roentgen Diagnosis of Tumors of the Breast, J. A. M. A. **105**:343 (Aug. 3) 1935.

11. Russell, T. H.: Personal communication to the author.

12. Lewis, D., and Geschickter, C.: (*a*) Ovarian Hormones in Relation to Chronic Cystic Mastitis, Am. J. Surg. **24**:280 (May) 1934; (*b*) Endocrine Therapy in Chronic Cystic Mastitis, J. A. M. A. **109**:1894 (Dec. 4) 1937.

13. Whitehouse, B.: Mastopathia and Chronic Mastitis, Surg., Gynec. & Obst. **58**:278 (Feb. 15) 1934.

14. Taylor, H. C., Jr.: Relation of Chronic Mastitis to Certain Hormones of the Ovary and Pituitary and to Coincident Gynecological Lesions: I. Theoretical Considerations and Histological Studies, Surg., Gynec. & Obst. **62**:129 (Feb. 1) 1936.

15. Semb, C.: Fibroadenomatosis Cystica Mammae, Acta path. et microbiol. Scandinav. (supp.) **5**:62, 1928.

PHYSIOLOGIC CONSIDERATIONS

The development of the breast with its activities has been conveniently divided by Turner [16] into six stages: (1) the embryonic and fetal period, (2) the interval between birth and puberty, (3) the period of recurring estrus cycles, (4) pregnancy, (5) lactation and (6) involution. Development of the mammary gland during the first two stages is the same in both sexes. With the approach of puberty and maturation of the ovaries, definite changes occur in the female breast; there is further growth of the duct system and of the connective tissue stroma. These changes, coincident with others elsewhere in the body, indicate the role of the mammary gland in the reproductive system. Disturbance in any of the reproductive organs invariably alters the development and function of the mammary glands. This was understood by Sir Astley Cooper [1] in 1829, when he hypothesized a causal correlation of disease of the uterus and other organs with certain morbid processes in the breast. In 1846 Brodie [4] called attention to the restriction of "sero-cystic tumors of the breast" to the period of sexual activity. These outstanding observations served as stimuli for further investigation.

Much interest has centered on the physiologic processes concerned with the menstrual cycle. Rosenburg [17] was the first to correlate histologic changes in the breast with changes in the ovaries. Others [18] also noted characteristic variations in the epithelium and in the connective tissue of the breast during the premenstrual, the menstrual and the resting stage of the monthly cycle. It has been observed that changes in the breast during menstruation are like those occurring during pregnancy but that they are present to a lesser degree. The glands increase in number, and there is hyperplasia of the epithelium and connective tissue stroma. If there is no conception, the gland returns to normal within two or three days after menstruation. Conception, however, with its concomitant physical changes, stimulates the breast to complete its development for ultimate function.

Until the close of the last century the nervous system alone was believed to be the factor coordinating the activities of the mammary glands with those of the ovaries, uterus and placenta. Studies on pregnant and nursing animals—through the isolation of the mammary

16. Turner, C. W.: Mammary Glands, in Allen, E.: Sex and Internal Secretions, Baltimore, Williams & Wilkins Company, 1932, pp. 544 and 583.

17. Rosenburg, A.: Ueber menstruelle, durch das Corpus luteum bedingte Mammaveränderungen, Frankfurt. Ztschr. f. Path. **27**:466, 1922.

18. (*a*) Dieckmann, H.: Ueber die Brustdrüse bei gestörtem und ungestörtem Menstruations-Ablauf, Virchows Arch. f. path. Anat. **256**:321, 1925. (*b*) Moskowicz, L.: Ueber den monatlichen Zyklus der Brustdrüse, Arch. f. klin. Chir. **142**: 374, 1926. (*c*) Litten, L.: Die histologischen Grundlagen der Sekretion nichtgravider Mammae, Virchows Arch. f. path. Anat. **259**:126, 1926.

gland from all nervous connections—seemed to prove the fallacy of this theory. Other avenues of investigation have since been followed, leading gradually to present theories of endocrine activity in the development of the breast not only during the prepubertal and pubertal periods, pregnancy and lactation, but during the climacteric as well. The ovarian hormones taking part in the initiation and in the final stages of the cycle are still subjects of debate among investigators.

ENDOCRINE INTERRELATION

The accompanying chart indicates hormonal influences, both known and suspected, affecting the breast. It is a composite drawing from various sources.[19]

Special interest has centered about the role of the anterior lobe of the pituitary gland in the endocrine cycle. Although much is still problematic, it is generally assumed that its influence is exerted through two of its gonadotropic substances, *A* and *B*, known respectively as the follicle-stimulating hormone and the luteinizing hormone. The *A* component activates the growth of the graafian follicle and its granulosal cells, to elaborate estrogen, a substance which experimentally produces estrus in rodents. Estrogen, in turn, in addition to producing edema and hyperemia, stimulates proliferation of the basal layer of the uterine endometrium (follicular phase, or follicular-endometrial stage). The *B* component, the luteinizing factor, stimulates the ruptured graafian follicle to formation of corpora lutea. Progestin, the active principle of the corpus luteum, is responsible for the secretory alteration of the previously estrogen-stimulated endometrium, which results in the characteristic premenstrual phase of the cycle (luteal phase, or luteal-endometrial stage).

Evidence of the lack of progestin is best shown by the fact that without follicular rupture the endometrium of the follicular (preovulation) phase does not advance to the luteal (secretory) phase, because if

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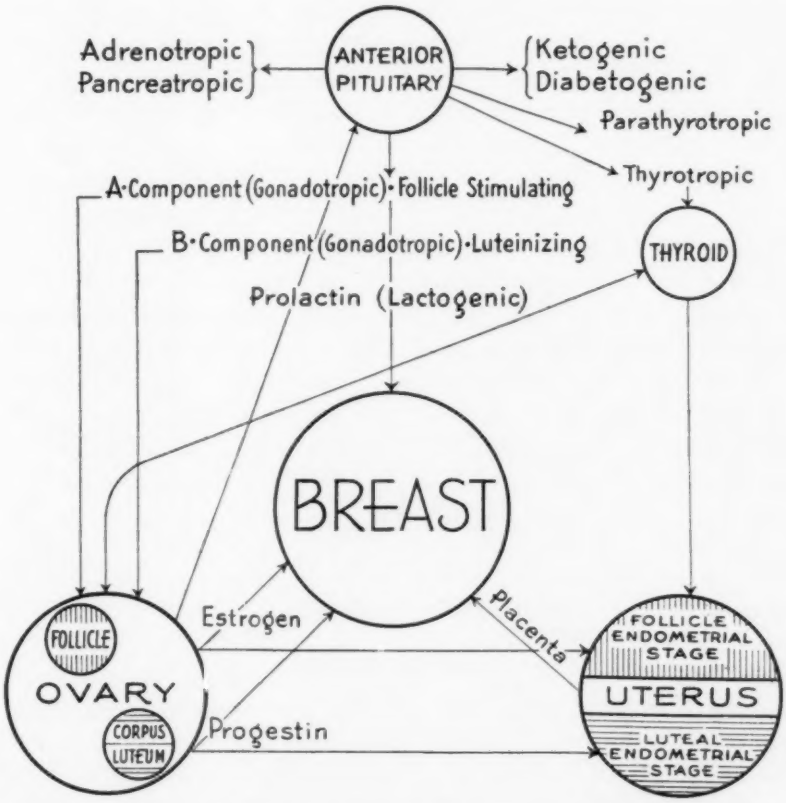
19. (*a*) Estrogenic Substances: Theelin, report of the Council on Pharmacy and Chemistry, J. A. M. A. **100**:1331 (April 29) 1933. (*b*) Heyd, C. G.: Hyperthyroidism, S. Clin. North America **5**:379 (April) 1925. (*c*) Frank, R. T., and Unger, A.: An Experimental Study of the Causes Which Produce the Growth of the Mammary Gland, Arch. Int. Med. **7**:812 (June) 1911. (*d*) Novak, E.: The Treatment of Primary Dysmenorrhea with Especial Reference to Organotherapy, Am. J. M. Sc. **185**:237 (Feb.) 1933. (*e*) Doisy, E. A.; Veler, C. D., and Thayer, S.: The Preparation of the Crystalline Ovarian Hormone from the Urine of Pregnant Women, J. Biol. Chem. **86**:499 (April) 1930. (*f*) Neustaedter, T.: Modification of Frank-Goldberger Blood Estrin Test, Endocrinology **20**:639 (Sept.) 1936. (*g*) Frank, R. T.: The Role of the Female Sex Hormone, J. A. M. A. **97**:1852 (Dec. 19) 1931. (*h*) Aschheim, S., and Zondek, B.: Hypophysenvorderlappenhormon und Ovarialhormon im Harn von Schwangeren, Klin. Wchnschr. **6**:1322 (July 9) 1927.

the follicle fails to rupture no corpus luteum is formed to supply the progestin. An atretic follicle results.

Based on the presence of definite amounts of estrogen in the blood and urine of normal fertile women, deviations from the normal may be determined during the menstrual cycle and climacteric period [19f, g] and during pregnancy.[20] When the concentration of estrogen in the blood reaches a peak, it inhibits the *B* component of the anterior lobe of the



Schematic diagram of the interrelations of the hormones affecting the breast.

pituitary gland. As a result, the corpus luteum degenerates and gradually ceases to function, finally becoming the corpus albicans. This occurs after ovulation with nonfertilization of the ovum and coincides with the onset of menstruation. Hence, the abrupt withdrawal of estrogenic substance is interpreted by some to be the initiating factor of menstrua-

20. Frank, R. T.; Goldberger, M. A., and Spielman, F.: A Method for Demonstrating the Prepituitary Maturity Hormone in the Blood of Non-Pregnant Women, Proc. Soc. Exper. Biol. & Med. **28**:999 (June) 1931.

tion, being manifested by the leukocytic invasion and collapse of the endometrial glands, desquamation and hemorrhage due to destruction of the capillary bed and to bleeding caused by rhexis. The premenstrual mammary syndrome usually also subsides at this time.

With fertilization of the ovum, however, the corpus luteum (corpus luteum of pregnancy) persists, and production of estrogen and progestin continues, the estrogen constantly increasing up to full term, whereas the progestin decreases after the sixth month. Mammary changes continue to the stage of lactation, after the decidua capsularis of the nidatory endometrium and the trophoblastic cells of the fertilized ovum become the placenta. Gonadotropic substance is recoverable from the urine during the period of gestation. The Aschheim-Zondek test [19h] is based on the presence of this substance in the urine.

The lactogenic substance (prolactin) of the anterior lobe of the pituitary has been identified and assayed.[21] It produces mammary hypertrophy such as is associated with pregnancy and lactation, but only in breasts previously subjected to the influence of estrogen.

It is not unlikely that aberrations in the reciprocal relation or disturbances in the equilibrium ratio of the various hormones may produce abnormal involution of the breast, giving rise to fibrocystic disease and its associated disturbances. Aschoff [6] characterized the disease as "preblastomatous [preneoplastic], dishormonal type," indicating the cause. Similar views were expressed by Franzas [22] when he wrote:

> The epithelial proliferation is probably activated by an abnormally altered sex hormone. For this to take place, a part, at least, of the gland parenchyma must be well enough preserved so that the pathological stimulus can reach the pathological threshold of epithelial proliferation.

CLINICAL MANIFESTATIONS

Fulness and enlargement of the breast are among the symptoms of fibrocystic disease, often associated with sensations of tingling to the point of actual pain, and recurring with notable regularity prior to or at the onset of menstruation. The pain in the breast is generally intermittent, and excessive tenderness may be present. In about 20 per cent of cases [23] pain radiates to the chest, shoulder or arm. Bleeding or

21. Riddle, O.; Bates, R. W., and Dykshorn, S. W.: The Preparation, Identification and Assay of Prolactin—A Hormone of the Anterior Pituitary, Am. J. Physiol. **105**:191 (July) 1933.

22. Franzas, F.: Ueber die Mastopathia cystica latenta und andere bemerkenswerte Veränderungen in klinisch symptomfreien weiblichen Brüsten, Arb. a. d. path. Inst. d. Univ. Helsingfors **9**:401, 1936.

23. Taylor, H. C., Jr.: Gynecological Aspects of the Etiology and Treatment of Chronic Mastitis, Surg., Gynec. & Obst. **57**:627 (Nov.) 1933.

discharge from the nipple may accompany these symptoms. The condition is usually bilateral; in older persons, however, it may be confined to one breast.

Fibrocystic disease may be without symptoms, as the work of Franzas [22] indicates. He investigated 200 breasts from 100 cadavers of women 18 to 90 years of age. All the women had been in a hospital for a longer or shorter time before death. None of the clinical symptoms of mammary disturbance had been present. In cases in which the history was defective, relatives of the deceased were questioned. Each breast, with areola and nipple, was divided into quadrants, and two sections were taken from each quadrant. When results were negative, Franzas took further sections from such breasts. For comparison, microscopic sections of the breasts of several dozen patients with fibrocystic disease (proved clinically) were used, as well as a number of various mammary tumors.

In 55 per cent of the 100 cases in which no symptoms had been present there were cyst formations similar to those of fibrocystic disease; in 25 per cent the condition was bilateral. In such cases of clinically latent disease, the connective tissue was not more prolific than in breasts not showing the cystic changes. Franzas failed to mention a comparison with connective tissue changes in clinically demonstrable fibrocystic disease. Schultz,[24] for example, wrote definitely of "the never-failing connective tissue increase . . . of the cystic breast." This increase in connective tissue, as compared with the absence of such increase in the latent form, may perhaps be linked to the fibrocystic disease becoming clinically manifest. Aschoff [6] also stated that this disease "may be called epitheliofibrous because it is representative of the irregular new growth of the glandular epithelium and of the connective tissues . . . ."

On palpation, the breasts may be practically normal in consistency or diffusely nodular, as in so-called "shotty breast." More often, however, there are moderately firm, irregular, freely movable masses, varying in size from 1 to 10 cm. Taylor [23] observed the appearance, intermittently, of a premenstrual lump in about 7 per cent of a series of 102 cases and a constant lump in about 11 per cent.

The age incidence varies, as observed by different authors. In the majority of 600 cases reported by Lewis and Geschickter [12a] the condition occurred in women between the ages of 35 and 45 years; in another series [18] of painful nodular breasts, the average age was 35 years. In approximately 80 per cent of Taylor's [23] series the patients were between 20 and 40 years; in 15 per cent, between 40 and 50 years, and

24. Schultz, A.: Die Zystenmamma, in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1933, vol. 7, pt. 2.

in 5 per cent, between 15 and 20 years. Fibrocystic disease of the breast is seen more frequently at an earlier age in nulliparae than in women who have undergone pregnancy and lactation. Although far less frequent than in the female, fibrocystic disease of the breast does occur in the male; 9 cases have been reported in which the condition occurred in male patients aged 14 to 48 years.[25]

PATHOLOGIC AND ANATOMIC PICTURE

There is a great difference of opinion as to the interpretation of the pathologic and anatomic character of the disease. Cheatle and Cutler [9] regarded the entire condition as one of "desquamative epithelial hyperplasia" which, they concluded, embraces two distinct states, differing widely both biologically and morphologically. These they called "mazoplasia" and "cystiphorous desquamative epithelial hyperplasia." Mazoplasia is defined as a process closely related to that of normal involution—a physiologic aberration which returns to normal at the menopause. The same condition may be found in the breast at birth and during pregnancy and lactation. There is desquamation of the epithelial cells of the terminal ducts and acini, accompanied by hyperplasia of the pericanalicular and periacinous connective tissue. Pain is attributed to distention of the acini and ducts, which are occluded by the accumulation of desquamated epithelial cells. In mazoplasia, the hyperplasia remains stable, forming neither cysts nor papillomas, being thereby distinguished from "cystiphorous desquamative epithelial hyperplasia" which Cheatle and Cutler identified as the condition usually referred to by others as "chronic cystic mastitis," Reclus' disease or Schimmelbusch's disease. In this cystic condition epithelial neoplasia may gradually develop—a process which likewise is never associated with mazoplasia. Cheatle and Cutler concluded that fibroadenoma, which occasionally forms, is the only lesion which may be ascribed to mazoplasia.

Whitehouse [13] was among those who disagreed with Cheatle and Cutler. In a pathologic and anatomic study of a large series of cases in which the condition was classified as "chronic mastitis," he reported the following findings and conclusions: 1. The condition described as "mazoplasia" is commonly associated in the same organ with the lesion described as "cystiphorous hyperplasia." 2. In both lesions epithelial hyperplasia is the preliminary dominant factor, and in both large numbers of pathologic lymphocytes are constantly present. 3. "Mazoplasia" in the adult appears to be the natural result of excessive stimulation of the mammary epithelium by the luteal hormone. 4. This

25. Campbell, O. J.: Relationship Between Cystic Disease of the Breast and Carcinoma, Arch. Surg. **28**:1001 (June) 1934.

excessive stimulation results in production of excessive secretion followed by cystic disease, the formation of cysts apparently representing a breakdown in the normal balance between production and absorption. The fluid from these cysts was found to contain colostrum cells and epithelium in the process of autolysis, but no fibrin. No coagulation occurred. Fat was found in some specimens, while others contained urea and uric acid. Because he regarded "mazoplasia" as a disorder of function, Whitehouse concluded that it is pathologic and not physiologic, even if it is a frequent condition.

Lewis and Geschickter [12a] studied human material obtained at definite periods during the menstrual cycle and pregnancy, as well as tissue from experimental animals after injection of estrone (theelin) and progestin. They concluded that "chronic cystic mastitis"—which they classified as (1) cystic disease of the breast and (2) as adenosis of the breast—corresponds to alterations in the character, amount or periodic discharge of the ovarian hormones, estrogen and progestin. An analysis of 600 cases of this condition is reported in support of their theory.

As has been stated, the pathologic-anatomic picture of the disease, as viewed by me, embraces three distinct types instead of the two outlined by Lewis and Geschickter.[12b]

In the cystic type of the condition there are dirty gray, firm, slightly elastic areas, not always well limited. A variable number of cysts are present, the individual cyst varying in size from that of a split pea to that of a walnut. Because of the translucency of the cyst wall, many unruptured cysts appear blue—"blue-domed" cyst, so named by Bloodgood.[8b] The content of the cyst varies; it may be clear and fluid or thick and creamy. It is never bloody as in a papillomatous cyst. The ducts are at times greatly dilated with material resembling Camembert cheese, composed largely of cast-off epithelium.

The most common microscopic picture (perhaps representing an early stage of the disease) is that of a double outline to the cells lining the glands or ducts. Another picture includes a lining of closely packed, multilayered polyhedral epithelial cells. These may form papillomatous projections into gland or duct spaces and may even unite with those of the opposite side to form bridges. The proliferating epithelial cells may completely fill the lumen. Not infrequently, so-called pale epithelium may be seen; in this the cells are cuboidal, staining pink with eosin (normally the cell body is more neutrophilic). The cytoplasm has the appearance of being composed of fine droplets. The pale character and shape of the cells strongly suggest sweat gland epithelium.

The histologic appearance may vary in different portions of the same specimen, and to obtain a complete picture it is essential to examine several sections. There may be epithelial hyperplasia, dilatation of the

lactiferous ducts (cyst of Brodie) or increase in stroma as well as infiltrative cells, which are usually seen in the presence of inflammation. Although Schimmelbusch [7] concluded that there is an increase of the acini in single lobules, his view has not been generally accepted.[24]

The increase of connective tissue stroma in some areas may suggest fibroadenoma; Schultz [24] spoke of adenomatous nodules, or microadenoma, as well as of cystadenoma, papillary and intracanalicular, both single and multiple. In young persons this increase lends a characteristic firmness to the breast; the connective tissue is denser and more hyalinized than in the senile breast. When compared with the epithelial elements—glands and ducts which are lined by low columnar to cuboidal as well as by flattened epithelium—the connective tissue in certain areas may predominate. Cast-off cells and even cholesterol crystals from the lipoid elements of the epithelial cells may be found in the cystic spaces; at times foreign body giant cells may be seen about the crystals.

The relation of fibrocystic disease of the breast to carcinoma is still actively debated, notwithstanding the numerous investigations devoted to the problem. While some authors [26] have concluded that fibrocystic disease cannot be regarded as a forerunner of carcinoma, Aschoff [6] wrote that "On the soil of such dishormonal preblastomatous proliferations [fibrocystic disease], there can easily be implanted the true blastomatous formation, benign or malignant."

According to Cheatle and Cutler,[9] approximately 20 per cent of all carcinomas of the breast start within the lesion of the "cystiphorous desquamative epithelial hyperplasia." A cyst may be present during the end of the second and in the early years of the third decade of life; during the next decade it may gradually pass into a state of benign epithelial neoplasia; the same lesion may then develop into a carcinoma (usually during the late forties or early fifties).

Rodman [27] found carcinoma associated with "chronic cystic mastitis" in 15.5 per cent of 100 patients of various ages. Whether or not malignant tumor develops from the preexisting cystic disease is a question which he believes must wait on discovery of the actual cause of cancer.

Bloodgood [8a] in 1906 regarded "chronic cystic mastitis" as a precancerous state. In 1921, after years of study and follow-up of typical cases, he completely reversed his opinion.[8b] He concluded [28] that cancer

26. Lewis and Geschickter.[12b] Franzas.[22]

27. Rodman, J. S.: Chronic Cystic Mastitis: A Further Report on the Nature of the Process, Am. J. Surg. **28**:452 (May) 1935.

28. Bloodgood, J. C., in discussion on Geschickter, C.: The Early Literature on Chronic Cystic Mastitis, Bull. Johns Hopkins Hosp. **55**:256 (June) 1934.

is a much less frequent occurrence in a breast with this disease than in the normal, the pregnant or the lactating breast. Campbell,[25] on the basis of a follow-up system of from three to ten years in over 200 cases in which the condition was treated either by local excision or by simple amputation, arrived at the same conclusion. Trout[29] and Harvey,[30] among others, agreed with this opinion, the latter believing that the disease "is an entity in itself, and should be so considered." In one series[12b] of 1,048 cases, 523 were followed for five years. Of this number carcinoma developed in less than 1 per cent (4 patients).

The solution of this problem is difficult, not only because both fibrocystic disease and malignant tumor generally affect persons of middle age or persons still older, but also because the etiologic factors of both conditions are still undetermined.

CAUSES

Lack of natural drainage of the products of secretion in the breast, which otherwise find an outlet when the mouths of the mammary glands open more widely during lactation, was pointed out by Keynes[31] as a possible etiologic basis of "chronic mastitis." The significance of this observation lies in the fact that the disease occurs less often in normally lactating mothers than in those who have suffered interrupted pregnancies or miscarriages or in unmarried women. The chemical nature of the stagnating secretion and epithelial débris and the frequent presence of associated carcinoma in the same breast suggested that both conditions might be due to the same factor. The findings of Adair[32] seem to lend emphasis to the theory of Keynes. Analysis of cellular débris in a series of 200 cases of mammary cancer showed that it contained both lactic and butyric acid. According to Adair, "these are considered to be an important part of those irritating factors responsible for the tissue reactions resulting in hypertrophy, precancerous changes and eventually cancer." It is pertinent that, as among women with fibrocystic disease, only a small proportion (8.5 per cent) had a history of normal lactation or of lactation entirely free from accidental incidents leading to impaired drainage. His findings were corroborated experi-

29. Trout, H. H.: Carcinoma of the Breast: A Study in Etiology and Prognosis, Am. J. Surg. **24**:258 (May) 1934.

30. Harvey, S. C.: Chronic Cystic Mastitis as a Physiological Aberration and Its Significance in the Diagnosis and Treatment of Tumors of the Breast, Yale J. Biol. & Med. **7**:521 (July) 1935.

31. Keynes, G.: Chronic Mastitis, Brit. J. Surg. **11**:89 (July) 1923.

32. Adair, F. E.: Etiological Factors of Mammary Cancer in Two Hundred Women; Also a Control Study of One Hundred Normal American Women, New York State J. Med. **34**:61 (Jan. 15) 1934.

mentally; cancer of the breast was produced in 87 per cent of a group of mice by means of artificial stagnation.[33]

Fibrocystic disease of the breast is often coincidental with pathologic conditions of the pelvis, including inflammatory lesions, cysts, fibroids, displacements or prolapse; a beneficial effect on mammary symptoms or their complete elimination occurs in many cases with successful treatment of the pelvic condition. The process by which this relation is established is still open to question. Of importance is the fact that in many cases fibrocystic disease occurs in women of nervous or hysterical temperament and that exacerbations sometimes follow a shock or great excitement. In this connection one cannot fail to observe a rather general tendency at present to revert to the theory involving the nervous system in the activities of the mammary gland—a theory previously referred to and one which had apparently been disproved at the end of the last century. Recent discussions have been concerned with the process of lactation and its bearing on pathologic conditions of the breast. Nelson [34] in a résumé of recent contributions to the subject concluded that development of the breasts and initiation of the secretion of milk are apparently under purely endocrine control, but that a nervous mechanism (in the reflex stimulation of the hypophysis) is probably instrumental in the maintenance of lactation. Clinically it has been demonstrated that lactation occurs in response to hormonal stimulation by intramuscular injection of pituitary lactogenic substance (prolactin).[35]

The frequent aggravation of mammary symptoms at the onset of menstruation seems to point to an endocrine factor. Fibrocystic disease of the breast is observed frequently in women who menstruate at frequent intervals; this suggests a disturbance in the production of estrogen or in that of progestin. Such women are low in potency, because the cyclic bleeding is usually anovulatory. Under such circumstances the ovum does not leave the follicle, and a corpus luteum does not form to stimulate the development of a good pregravid (luteal) endometrium. Irregular menstruation and interrupted pregnancies are often associated with fibrocystic disease of the breast. A review of the literature leaves little doubt that such mammary changes

33. (*a*) Bagg, H. J.: The Role of Functional Activity in the Production of Mammary Carcinoma, Am. Naturalist **60**:234, 1926. (*b*) Adair, F. E., and Bagg, H. J.: Breast Stasis as the Cause of Mammary Cancer, Internat. Clin. **4**:19 (Dec.) 1925.

34. Nelson, W. D.: Endocrine Control of the Mammary Gland, Physiol. Rev. **16**:488 (July) 1936.

35. Kurzrok, R.; Bates, R. W.; Riddle, O., and Miller, E. G., Jr.: The Clinical Use of Prolactin, Endocrinology **18**:18 (Jan.-Feb.) 1934.

are the result of repeated and perhaps aberrant stimulation by progestin and by the associated substances estrogen and the pituitary lactogenic factor (prolactin).

DIAGNOSIS

Methods of determining the amount of estrogenic substance in the blood and urine [36] have greatly facilitated the diagnosis of underlying glandular disturbances. The tests are comparable to tests for determining the basal metabolic rate in functional disorders of the thyroid or to studies of calcium and phosphorus in disturbance of the parathyroid glands.

Transillumination and roentgen examination are additional methods of considerable value in the diagnosis of fibrocystic disease. With transillumination many of the larger "blue-domed" cysts and other mammary conditions of altered density are more readily recognized. In distinguishing a hematoma from a solid tumor transillumination is of great advantage.

Roentgenographic study is also helpful in determining the presence of a neoplasm.[10] In viewing the breast roentgenologically it is important to remember that the various phases of the menstrual cycle alter the anatomic features to a considerable degree; the same is true also of pregnancy and lactation.

Careful and practiced palpation affords one of the most valuable means of diagnosing lesions of the mammary gland. Preceded by an accurate history and preliminary inspection of the breasts under proper light, palpation translates changes in the skin or nipples, i. e., superficial irregularity, into specific underlying alteration of the tissues. This is best accomplished by lightly and delicately passing the finger tips radially over the entire breast by quadrants, from areola to periphery. A circumscribed tumor can usually be accurately outlined. Its mobility in relation to the tissues immediately adjacent aids in differentiating a discrete from an invasive neoplasm. Diffuse nodularity (adenomatosis) not infrequently can be distinguished from cyst formation, and gentle pressure along the ducts will occasionally express from the nipple secretions that in themselves are more or less diagnostic.

The axillary and clavicular areas, as well as the borders of the pectoralis and latissimus dorsi muscles, should be carefully palpated for involvement of the regional lymph nodes.

The posture of the patient during examination is extremely important. Frequently a "mass" felt between the thumb and fingers when the patient

36. Frank, R. T.: The Present Status of the Female Sex Hormone from the Clinical Standpoint, New York State J. Med. **34**:1009 (Dec. 1) 1934. Neustaedter.[19f] Frank, Goldberger and Spielman.[20]

is sitting and the breast is pendulous will disappear when the patient is prone and the breast is allowed to flatten itself to a "neutral disk" against the chest wall.

A combination of the three methods—transillumination, roentgenographic examination and palpation—may be necessary. These should be combined with a thorough general physical examination, special attention being given to possible pelvic disorders. A careful menstrual history must be included in each case.

A characteristic feature of this disease is the simultaneous occurrence of two or more lesions in the same breast. These include papillomatous cyst, blue dome cyst, adenoma, adenofibroma, cystadenoma and carcinoma. Microscopic study of repeated frozen sections from different areas is clearly indicated in such cases.

Bloodgood [37] suggested analysis of the contents of the various lesions as a means of differentiation. He pointed to the presence of blood as indicative of papillomatous cyst or of carcinomatous cyst and to its absence in blue dome cyst. Another distinguishing feature is the fact that the blue dome cyst is never grumous, as is the carcinomatous cyst, nor does it contain pus as does the tuberculous abscess or the abscess associated with chronic lactational mastitis.

A bloody or serous discharge from the nipple, while not a frequent occurrence, may likewise serve as a diagnostic aid. From a study of records of patients with mammary disease who had been treated for several years, Stowers [38] found that a discharge of blood from the nipple, with no palpable tumor and with no history of trauma, presumably indicates a papilloma of a duct or ducts of the breast. A so-called purulent discharge from the nipple in his series was associated with "cystiphorous desquamative epithelial hyperplasia" or with carcinoma. A discharge of serum or blood from the nipple, with or without a papable tumor, points to a surgical condition.

In establishing the presence of "premalignancy" or "early malignancy," biopsy must be undertaken. Of paramount importance is the question of "premalignancy." Features such as highly atypical shape, size and staining power of the proliferating gland and duct cells, solid nests in the lumens, connective tissue increase subdividing the bands of epithelium without true invasion of the connective tissue by the neoplasm or the occurrence of numerous mitoses are frequently considered as representing a premalignant phase. Some [26] are of the opinion, how-

37. Bloodgood, J. C.: The Blue-Domed Cyst in Chronic Cystic Mastitis: Its Relation to the Cure of Cancer, to Benign Lesions of the Breast, and to the Educational Program, J. A. M. A. **93**:1056 (Oct. 5) 1929.

38. Stowers, J. E.: The Significance of Bleeding or Discharge from the Nipple, Surg., Gynec. & Obst. **61**:537 (Oct.) 1935.

ever, that there is no indication that a picture representing these features definitely precedes cancer of the breast. The term "premalignant" has been so greatly abused that many pathologists avoid its use if the microscopic picture as described in such a disease is caused by abnormal endocrine influences. "Premalignant" indicates that there is growth activity of the epithelial cells and that the fibrocystic disease is serious. Accurate statistics are lacking, but Aschoff [6] was "persuaded that a precancerous state degenerates into carcinoma in the course of years, not decades . . . ." If, however, the hyperplastic epithelium extends into the surrounding connective tissue stroma, disturbing the normal outline of the base of the epithelial cells against the stroma, the condition is definitely carcinoma. What is usually called "early malignancy" is carcinoma which has not grown extensively. It may have been growing slowly. Hence, "early" is highly inappropriate. It is the breakdown of the usual restrictions of tissue order or structure which indicates malignancy. Carcinoma and fibrocystic disease may both be present, and it is generally necessary to examine several sections before the carcinoma is located.

TREATMENT

Considering the varied nature of the symptoms and the pathologic and anatomic picture that may be presented, as well as the fact that a definite etiologic basis for fibrocystic disease is still unknown, it is obvious that treatment must be adapted to the individual case.

When pain is the predominant symptom and is confined to the upper limits of the breast (pain due to actual weight or drag of a pendulous breast) adequate support or uplift will generally provide prompt relief. In other cases removal of foci of infection will often result in improvement of the mammary condition. Roentgen irradiation of the ovaries may be of benefit, although this method is applicable only to a limited group. Diathermy, short wave therapy and moist heat have received comparatively little attention.

When pelvic disorders occur in association with fibrocystic disease the pelvic condition should be treated first. Many patients require no other therapy, the mammary condition soon responding to improvement or cure of the pelvic condition. A similar interdependence exists throughout the entire endocrine system, the thyroid, parathyroid, pituitary, adrenals, ovaries and mammary glands, among others, being directly or indirectly included. In case of amenorrhea of thyroid origin accompanied by fibrocystic disease, thyroid substance will, as a rule, favorably influence the amenorrhea [39] and, in turn, will often entirely

39. Novak, E.: The Therapeutic Use of Estrogenic Substances, J. A. M. A. **104**:1815 (May 18) 1935.

clear up the fibrocystic disease. Amenorrhea, however, does not in all cases respond to this form of glandular therapy.

Other forms of glandular therapy have been advocated, from time to time, for the treatment of fibrocystic disease.[40] Corpus luteum, which had previously been employed in eliminating or ameliorating disagreeable symptoms of the menopause, was administered two decades ago [41] for the treatment of mammary pain accompanying menstruation. Cutler [42] from an opposite point of view, concluding that the condition of "painful breasts" is due to overstimulation by the corpus luteum, administered ovarian residue by mouth for the purpose of increasing the deficient follicular and interstitial elements of the ovary and thus counteracting the overactive corpus luteum. Whitehouse [13] for the same purpose of counteracting the corpus luteum and, in addition, of preventing mammary stagnation administered an estrus-producing substance, estrone (theelin) daily by injection during the premenstrual period. Lewis and Geschickter [12b] recently reported the successful treatment of "painful breasts," the condition being characterized by them as an early stage of cystic disease. An estrogen was given intramuscularly twice a week for several months. Although favorable results were obtained in "adenosis," lasting results in the presence of cysts were more difficult to obtain.

I have tried treating patients with fibrocystic disease by various means. The oral administration of ovarian residue, as advised by Cutler,[42] was disappointing. Few, if any, similar substances were of value when given orally, inasmuch as the action of the gastric juices on them makes exact dosage impossible. The hypodermic administration of a gonadotropic substance from the placenta (A. P. L.) has given the most favorable results, producing relief of pain and subsidence of palpable alterations in the breast.

Discrete masses, solid or cystic, should be removed surgically by simple excision of the mass. When not obviously benign or grossly malignant, the neoplasm should be subjected to immediate histologic (frozen section) examination to determine the necessity for more extensive surgical treatment. Diffuse fibrocystic involvement of one or both breasts, however, does not lend itself so readily to multiple excisions. Owing to the widespread distribution of the process as demonstrated by serial sections, total ablation of mammary tissue (simple

40. Goodman, B. A.: Glandular Therapy in Diseases of the Breast, S. Clin. North America **12**:539 (April) 1932.

41. Lisser, H.: A Note on the Use of Corpus Luteum to Prevent Painful Breasts of Menstruation, Endocrinology **2**:12 (Jan.) 1918.

42. Cutler, M.: Cause of "Painful Breasts" and Treatment by Means of Ovarian Residue, J. A. M. A. **96**:1201 (April 11) 1931.

mastectomy) is sometimes necessary. When possible, however, opportunity should be given for other measures, especially endocrine therapy, to prove their inadequacy before resorting to operation.

SUMMARY

1. The term "fibrocystic disease of the breast" is suggested to cover and possibly to replace the diverse terms applied to a group of conditions referred to as abnormal involution of the breast, cystic disease of the breast, Reclus' disease, serocystic tumor of the breast, chronic cystic mastitis, cystadenoma, Schimmelbusch's disease, senile parenchymatous hypertrophy, mazoplasia, cystiphorous desquamative hyperplasia, cystoplasia, cystic disease of the breast, mastopathia, adenofibrosis and fibroadenomatosis. The choice of the term "fibrocystic disease of the breast" rests on its definite characterization of the outstanding features of the condition—the fibrous and cystic elements.

2. The disease is a nonstatic condition the clinical and microscopic pictures of which are varied.

3. That fibrocystic disease of the breast is in the beginning essentially a functional disorder of the nonlactating breast, which assumes certain pathologic characteristics as a result of repeated and possibly aberrant stimulation by the luteal hormone progestin and the associated hormones estrogen and prolactin (the lactogenic substance of the anterior lobe of the pituitary) is a tenable hypothesis. If one accepts the stagnation theory of Keynes,[31] it is possible to trace a series of events beginning with proliferation in the breast, including cyclic changes produced by menstruation and lactation, and continuing through the various states of the disease—the cystic and papillomatous stages and, possibly, a malignant stage.

4. Treatment in each case must include a careful history, a period of competent observation and elimination of focal infection and concomitant pelvic disorders. In many cases treatment with potent estrogenic substances has proved efficacious. A chorionic derivative (anterior pituitary-like principle) seems at present to be most effective.

5. Continued investigation of the interrelations of the endocrine glands and qualitative and quantitative determinations of the various endocrine substances are essential, for therein lies the promise of a better understanding of the pathologic processes involving the human breast.

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RATE OF FIBROPLASIA AND DIFFERENTIATION IN THE HEALING OF CUTANEOUS WOUNDS IN DIFFERENT SPECIES OF ANIMALS

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In the healing of wounds of muscle, fascia, skin and gastric wall of the dog, strength returns in a definite manner. During the first four days, the wounds have only the strength contributed by the sutures and the adhesion of the wound surfaces; subsequently, however, strength mounts rapidly, reaching a maximum on the twelfth to the fourteenth day of healing.[1] This increase in strength is accompanied microscopically by regeneration of fibrous tissue; hence, strength is used as an index to the rate of fibroplasia. Because the rate of fibroplasia is the same in the healing of these diversified anatomic structures, it has occurred to us that the rate should be studied in the healing of wounds of one tissue in several species of animals. In this way any influence on the rate of fibroplasia due to differences in species could be determined. In the experiments described here, therefore, the relation of species differences to the rate of fibroplasia has been studied by testing the strength of healing wounds in the skin of the usual laboratory animals. Particular attention has been directed toward the question whether the wounds actually return to the original strength of the skin injured.

METHOD

Under strictly aseptic precautions, wounds approximately 4 cm. in length were cut in the skin of the abdomens of anesthetized rats, guinea pigs, rabbits, cats and dogs. The ends of each wound were marked subcutaneously with silk to indicate the extent of the wound when the tissues should be removed. The edges were approximated with interrupted A silk sutures, subsequently removed after a week of healing (or earlier when the strength of the wound was determined earlier).

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1. Howes, E. L.; Sooy, J. W., and Harvey, S. C.: The Healing of Wounds as Determined by Their Tensile Strength, J. A. M. A. **92**:42 (Jan. 5) 1929.

The wounds were periodically inspected for infection, and only those healing per primam were ever tested for strength. For the test a strip of tissue was excised at right angles to the wound. This strip was of no greater width than the length of the wound. It was cut sufficiently long so that it might be secured in the clamps of the tensile strength machine. The thickness and width of each wound were measured after the strip was put under a tension of 100 Gm. in the tensile strength machine.[2] Tests of strength were made every day or every other day during

TABLE 1.—*Breaking Strength of Cutaneous Wounds*

Guinea Pig			Rat		
Day	Number of Animals	Av. in Gm. per Sq. Mm.	Day	Number of Animals	Av. in Gm. per Sq. Mm.
4	2	0	3	4	1
6	1	45	4	4	6
7	3	37	5	45	15
8	1	151	6	4	23
9	2	99	7	2	40
10	1	137	8	3	98
14	1	155	10	44	99
16	2	102	12	2	148
20	3	174	13	3	157
22	1	114	14	4	143
24	1	162	15	39	175
26	2	124	17	2	134
28	2	139	18	3	163
30	1	186	20	42	263
33	2	301	22	3	299
35	2	187	24	4	417
36	1	564	27	4	450
38	2	263	30	34	573
40	2	309	32	2	472
60	1	1,723	34	2	608
65	1	353	35	1	579
70	1	470	36	6	656
143	1	1,255	37	1	850
200	1	2,225	38	2	778
250	2	1,994	40	33	572
			42	3	800
			45	4	855
			50	31	791
			52	2	694
			53	2	1,007
			56	2	855
			58	2	782
			60	2	1,261
			64	2	1,052
			67	2	1,441
			70	2	1,036
			74	1	1,709
			77	2	745
			80	19	999
			90	1	1,516
			100	2	1,440
			127	1	1,314
			152	2	1,684
			178	1	1,232
			210	2	2,092

the first twenty days of healing but at less frequent intervals in the subsequent weeks. The strength of the wound was calculated for a unit of area (tables 1

2. The measurement of the tissues presented a problem. If the width of the wound was measured in situ, thickness could not be measured accurately, and small variations in this diameter markedly affected the results. On the other hand, if the tissue was removed, the tension applied to the strip and its direction of application changed the dimensions. However, with the same distortion applied to each strip, measurements were obtained of sufficient accuracy to allow a comparison of the results.

and 2); the corrected strengths were plotted as a function of time. The resulting curves are shown in figures 1 and 2. At frequent intervals the character of healing was studied microscopically and correlated with the changes in strength of the wound. Normal skin from the different animals was also tested for strength and cut for microscopic study.

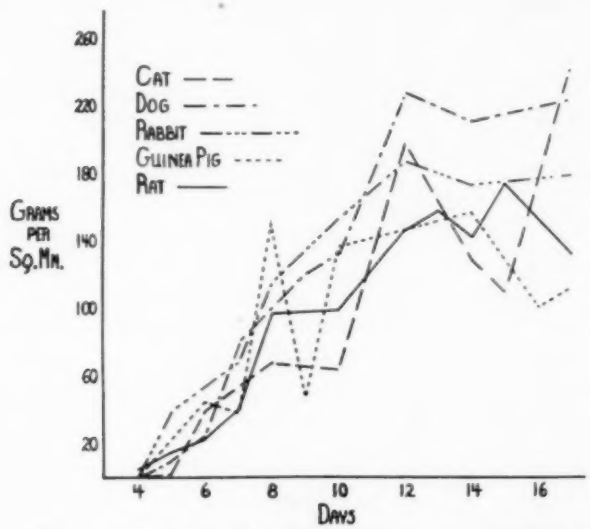

Fig. 1.—Early breaking strength of cutaneous wounds.

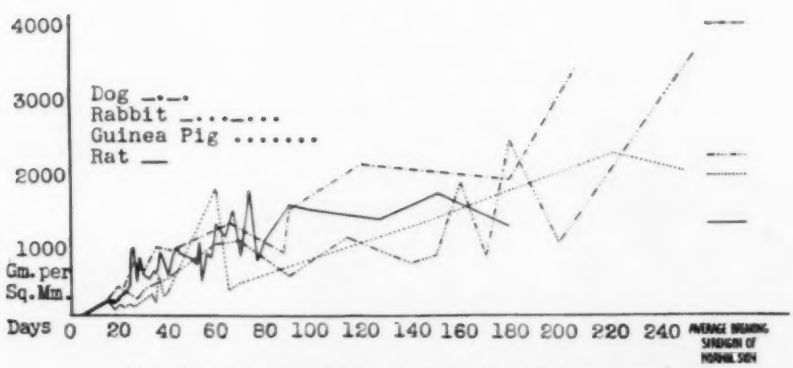

Fig. 2.—Later breaking strength of cutaneous wounds.

STRENGTH OF NORMAL SKIN

The strength of the normal skin of different animals is shown in table 3. The variation in strength was not all caused by error in the method of testing, for it occurred in a distribution typical of biologic variations. The amount of variability occasioned by the method can be approximated from an inspection of the first five values in the table

for the rat, all obtained from the same skin. The greater average strength of the skin per unit of area occurred in the larger animals. In general, skin has a fair degree of strength, a physical property in consonance with its function as protector of the organism from the environment. The data furnished by Gratz [3] allow a comparison of the strength of the skin with that of other fibrous structures of the body. He has shown that tendon and fascia in the dog have an average strength of about 5,000 Gm. per square millimeter, while that of the skin of the same animal, from our experience, is approximately 4,000. The

TABLE 2.—*Breaking Strength of Cutaneous Wounds*

Rabbit			Dog			Cat		
Days	No. of Animals	Av. in Gm. per Sq. Mm.	Days	No. of Animals	Av. in Gm. per Sq. Mm.	Days	No. of Animals	Av. in Gm. per Sq. Mm.
5	2	39	4	1	0	5	3	2
7	3	68	5	3	10	6	1	39
8	2	115	6	1	23	8	6	68
10	3	154	7	1	80			
12	2	188	9	1	120	12	4	200
14	5	175	10	2	133	14	2	129
17	2	181	12	2	230	18	1	495
19	1	195	14	4	213	20	1	348
22	1	329	17	1	225	30	1	532
27	1	236	19	1	415			
30	1	342	21	1	376			
40	1	509	26	1	721			
60	1	969	30	1	602			
70	1	1,018	35	1	930			
80	1	794	42	1	880			
90	1	537	66	1	1,275			
100	1	779	87	1	871			
115	1	1,062	90	3	1,430			
120	1	1,627	120	1	2,068			
140	1	709	180	1	1,852			
150	1	827	207	1	3,348			
160	1	1,784	345	1	2,223			
170	1	801	353	1	1,580			
180	1	2,356	358	1	2,271			
200	1	1,022						
255	1	3,595						

strength of the skin is in the main derived from the corium, which is composed of heavy collagenous fibers intertwined and running in many directions (figs. 3 and 4).

COMPARISON OF STRENGTH OF THE HEALING WOUND IN VARIOUS SPECIES

In all the wounds, strength began to mount on the fifth day and continued to increase at the same rate, slowing to reach a maximum on

3. Gratz, C. M.: Biomechanical Studies of Fibrous Tissues Applied to Fascial Surgery, Arch. Surg. **34**:461 (March) 1937.

TABLE 3.—*Breaking Strength of Normal Skin in Grams per Square Millimeter*

Rat		Guinea Pig	Rabbit	Dog	Cat	
950	414	1,136	2,273	2,591	6,427	
1,045	755	3,123	2,841	4,127	4,036	
1,227*	468	1,075	2,300	3,195	2,968	
1,000	400	1,223	1,700	4,777	3,541	
1,272	845	2,023	2,436	3,364	7,736	
1,323	873	1,914	1,700	4,364	3,636	
	1,218	2,550	1,331	3,168	6,563	
2,273	1,077	1,432	3,050	3,009	8,471	
1,845	1,014	1,541	2,041	2,504	4,300	
2,165	741	1,182	2,050	1,873	5,801	
2,000	1,077	2,254	1,218	6,627	4,545	
1,277	664	1,791	2,841	5,491	6,059	
1,818	627	2,727	1,500	5,554	5,191	
1,364	1,705	2,145	1,705	3,304	1,109	
1,555	1,295	1,373	1,091	4,091	5,150	
1,464	995	1,859	3,500	7,805	5,495	
1,273	1,259	1,664	2,045	3,445	12,063	
1,136	1,595	1,973	1,955	4,341	8,413	
864	1,495	1,173	2,636	3,650	9,259	
1,559	2,368	1,814	2,423	7,727	.....	
704	1,023	414	1,577	2,709	.....	
291	673	2,172	1,590	3,000	.....	
1,150	1,205	45	6,759	4,759	.....	
1,318	1,618	50	1,532	3,468	.....	
982	1,486	2,186	3,359	.....	.....	
295	1,795	1,281	3,818	.....	.....	
668	1,814	2,000	1,627	.....	.....	
890	1,818	990	1,418	.....	.....	
964	2,650	1,350	1,354	.....	.....	
1,623	1,559	1,400	2,704	.....	.....	
1,364	2,000	695	422	.....	.....	
.....	.....	227	.....	.....	.....	
.....	.....	1,577	.....	.....	.....	
.....	.....	605	.....	.....	.....	
.....	.....	1,545	.....	.....	.....	
.....	.....	1,514	.....	.....	.....	
.....	.....	981	.....	.....	.....	
.....	.....	2,231	.....	.....	.....	
.....	.....	1,481	.....	.....	.....	
.....	.....	5,490	.....	.....	.....	
.....	.....	6,627	.....	.....	.....	
.....	.....	5,554	.....	.....	.....	
.....	.....	3,304	.....	.....	.....	
Mean.....	1,254	1,909	2,127	3,931	5,858	Normal average
Standard deviation of mean.	68	172	190	309	574	

* From the same animal.

TABLE 4.—*Breaking Strength of Cutaneous Wounds at End of Fibroplasia in Grams per Square Millimeter*

Rat at 15 Days		Guinea Pig at 14 Days	Rabbit at 14 Days	Cat at 14 Days	Dog at 14 Days
195	136	95	264	150	182
91	209	245	377	105	255
105	227	127	254	114	200
155	191	...	91	...	255
100	318	...	95	...	236
191	77	...	132	...	141
214	182	...	214	...	227
277	227	...	164	...	314
273	164	...	105	...	105
205	130	...	45	...	...
136	136	...	205	...	...
91	116	...	155	...	...
141	241	...	...	...	...
282	138	...	...	...	...
77	173	...	...	...	...
118	179	...	...	...	...
182	195	...	...	...	...
291	136	...	...	...	...
186	102	...	...	...	...
236	...	...	...	...	...
Mean.....	175	156	175	126	212
Standard deviation of mean	9.9	37.1	15.7	13.7	16.0
Variations in average.....	18.4	193	190	139	228
Calculated with standard deviation.....	16.6	119	100	113	198
Percentage of original strength.....	13	8	8	2	5

the twelfth to the fourteenth day of healing (fig. 1). The rate of fibroplasia was not affected by differences in species. At the end of the period of fibroplasia the normal strength of the skin was not regained. In the rat, 13 per cent of the strength was restored, in the rabbit 8 per cent, in the cat 2 per cent and in the dog 5 per cent (table 4). The percentage variations in strength resulted more from the difference in the original strength of the skin injured than from the difference in the strength of the new fibrous tissue. The spread of original strength of the skin is compared with the grouping of the strength of the wounds in figure 2. This grouping suggests that the tissue produced by fibro-

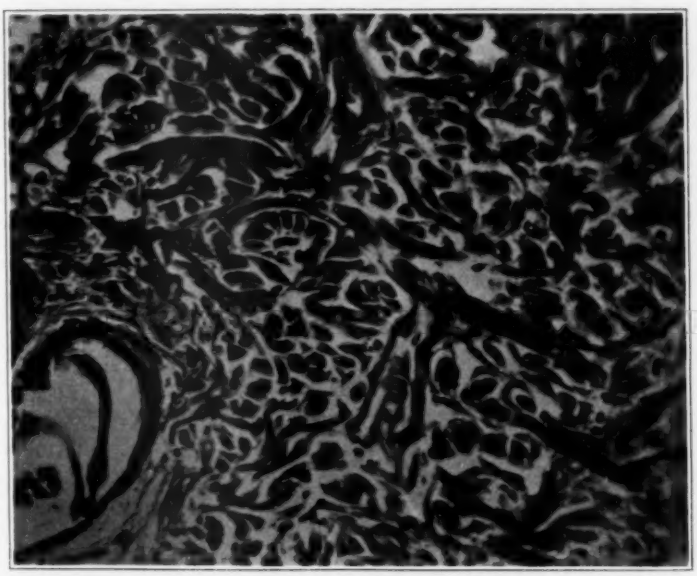

Fig. 3.—Collagenous fibers (× 200) of the normal corium of the rat.

plasia has the same strength per unit of area. In each wound the tissue was relatively undifferentiated, was of homogeneous density and was composed of fine parallel fibers with numerous fibroblasts between. It was vascular and had a loose arrangement of stroma (figs. 5, 6 and 7). The average strength in each wound, with the possible exception of that of the dog, was within the range of error of the experiment.

The anatomic explanation as to why the wound had not returned after the process of fibroplasia to the original strength of the skin injured was found in the difference between the embryonal-like tissue produced by the process and the well differentiated, heavy and compact collagenous fibers of the original corium (figs. 3 and 4).

A secondary rise in strength of the cutaneous wounds of the different animals occurred at approximately the same time in each. It is present on the twentieth day in the rat, on the twenty-second day in the rabbit and on the eighteenth day in the cat, and although earlier experiments [1]

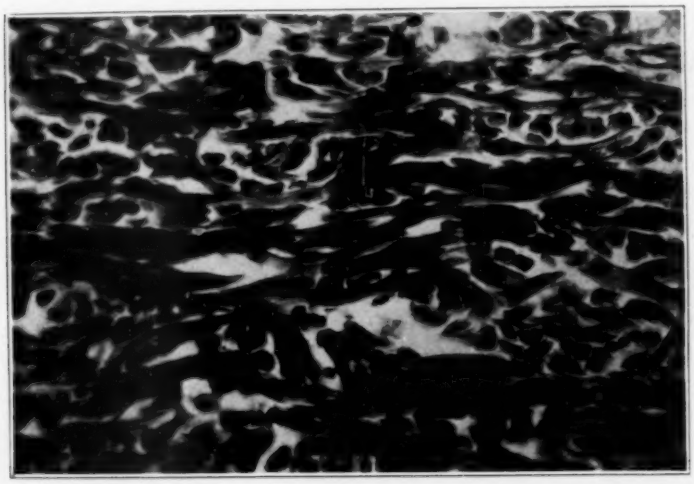

Fig. 4.—Collagenous fibers (× 200) of the normal corium of the dog.

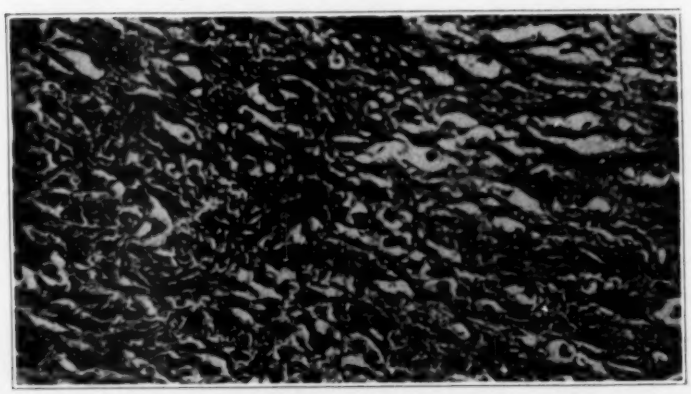

Fig. 5.—Fibrous tissue (× 200) resulting from fibroplasia. A dog was used in this experiment. The photomicrograph was taken when the wound was fourteen days old.

suggested that the rise might occur later in the wound of the dog, it appeared in this animal on the nineteenth day. On the other hand, in the wound of the guinea pig it was delayed until the thirtieth day.[4]

4. The guinea pig was found to be the poorest laboratory animal for these experiments. The usual percentage of wounds healing per primam was not obtained with this animal.

Through this secondary rise in strength, the scars [5] ultimately regain approximately the original strength of the skin injured (fig. 2). This secondary increase in strength is accompanied anatomically by an organizing differentiation of the primary tissue produced by the fibroplasia.

Fig. 6.—Fibrous tissue (× 200) resulting from fibroplasia. A rat was used in this experiment. The photomicrograph was taken when the wound was fourteen days old.

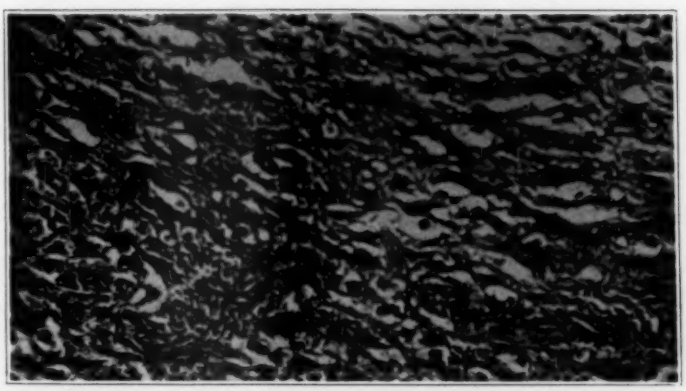

Fig. 7.—Fibrous tissue (× 200) resulting from fibroplasia. A guinea pig was used. The photomicrograph was taken when the wound was fourteen days old. The round spots are not fibers cut in cross section but lymphocytes.

The fine fibrils increase in size, and more of them run in directions other than parallel (figs. 8, 9 and 10). The sizes of the collagenous

5. "Scar" seems the proper word at this time, for the wounds are healed in the usual sense of the term.

fibers more and more approximate but never equal the dimensions of those of the original corium. The round cells and blood vessels of the primary tissue gradually disappear. Fewer elastic fibers are present,

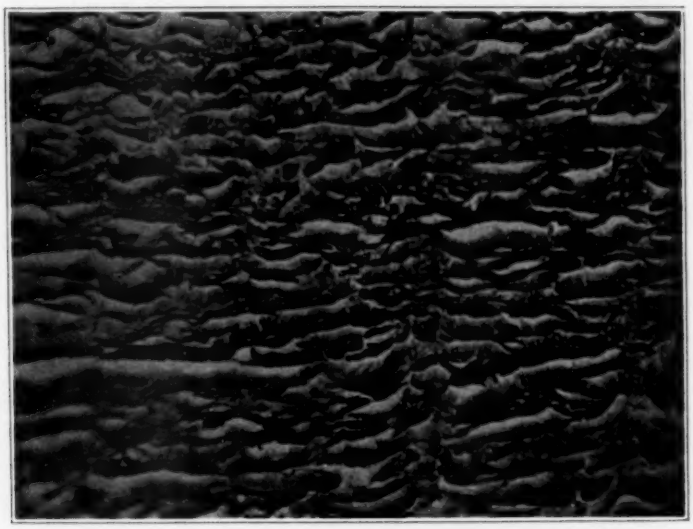

Fig. 8.—Fibrous tissue (× 200) of the scar of a fifty-one day old wound. A rat was used.

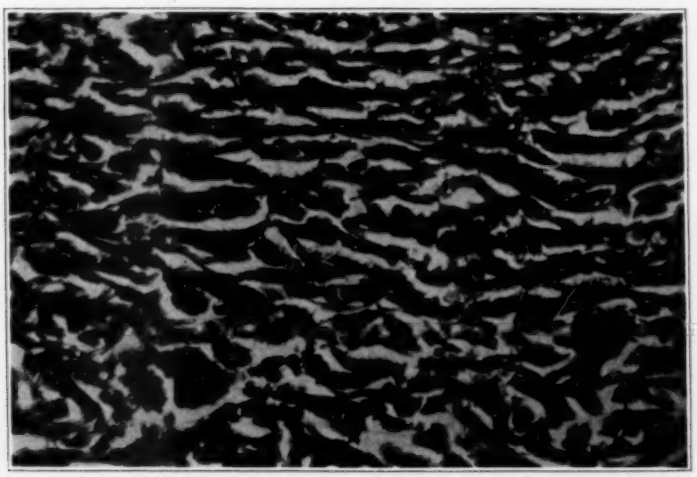

Fig. 9.—Fibrous tissue (× 200) of the scar of a ninety day old wound. A guinea pig was used.

and these are short and thick. The entire architecture is differentiated without a vestige of embryonal pattern. The collagenous fibers, however, are more rudimentary and more compact than in the original

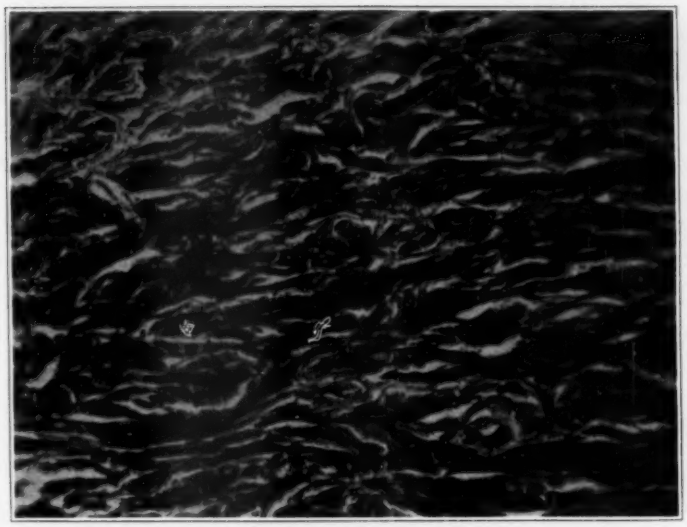

Fig. 10.—Fibrous tissue (× 200) of the scar of an eighty-two day old wound. A rat was used.

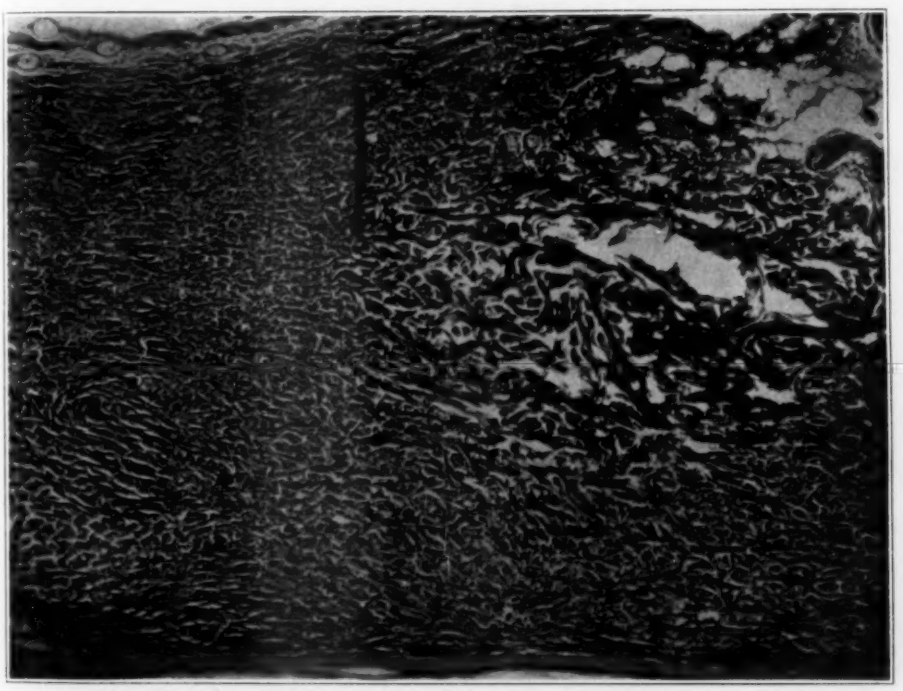

Fig. 11.—Scar left by the experimental wound (× 95). Note the normal corium at the right. The experimental animal was a rat. The photomicrograph was taken one hundred and fifty-eight days after the experiment.

corium, and the picture does not completely resemble the normal but closely approximates it (fig. 11).

The rate of differentiation, as judged by the increase in the strength of the scars per unit of area, is not of unusual velocity in any particular species (fig. 2). Yet the original strength of the skin is regained after varying lengths of time. These variations must be attributed to the differences in the ultimate strength to be regained. For example, with differentiation proceeding at the same rate in the scars of the rat, the rabbit and the guinea pig and the ultimate strength needed being 1,200 Gm. per square millimeter in the skin of the rat, 2,170 Gm. in the rabbit and 3,930 Gm. in the dog, it is understandable that the strength of the scar becomes as great as that of normal skin after sixty days in the rat and after one hundred and eighty days in the rabbit and that after three hundred and fifty-eight days the original strength is not completely regained in the scar of the dog (tables 1, 2 and 3 and fig. 2).

COMMENT

The character and rate of fibroplasia were the same in the healing of cutaneous wounds of the different species of animals studied. From the results obtained, together with the previous data on the character and a similar rate of fibroplasia in the healing of wounds of different tissues of the same animal,[1] the conclusion must be reached that the process of fibroplasia is an independent biologic phenomenon unrelated to the kind of tissue or the species wounded and corresponding to the general laws of growth. This has been discussed elsewhere.[6]

The more rapid gain of strength after the period of fibroplasia in the healing of wounds in the smaller animals has given origin to the concept that their wounds heal faster than do those of larger animals. Actually, however, the greater gain is accomplished not because of an increased rate of fibroplasia and differentiation but because less strength is ultimately needed to reach the normal.

While the normal strength of the skin is not regained in the period of active fibroplasia, the original strength of muscle, gastric wall and fat is so restored.[1] The reason for this is that the normal strength of these structures is no greater than that developed by proliferation of fibroblasts alone, while in structures such as skin, bone, tendons and fascia an organizing differentiation is required for a restoration of the much greater normal strength. Thus, the healing of structures originally possessing greater strength than the tissue regenerated by fibroplasia is accomplished by the generation of a "primary callus," which rapidly establishes the continuity and which must be differentiated later to

6. Harvey, S. C.: Reaction to Injury as a Function of Growth, Proc. Inst. Med. Chicago **10**:70 (April 15) 1934.

approximate the original function. The excess of primary tissue disappears with differentiation, but wounds healing in this manner remain comparatively weak until differentiation is completed. The more strength the tissue possesses originally, the longer will be the period of relative weakness.

CONCLUSIONS

1. The rate of fibroplasia is the same in the healing of cutaneous wounds in the rat, the guinea pig, the rabbit, the dog and the cat, and the difference of species does not affect the rate.

2. The period, approximately two weeks, during which fibroplasia occurs is an independent biologic phenomenon unrelated to the species or type of tissue wounded and corresponds to the process of growth.

3. The tissue of the wound does not return to the normal strength of the skin except by a prolonged period of differentiation of the tissue produced in this initial period.

4. The velocity of differentiation as estimated by the secondary increase in the strength of the wound is the same for the different species of animals investigated.

5. Nevertheless, the time when the scars attain the original strength varies in different animals. The variations are occasioned by differences in the strengths which have to be attained in order to reach the normal, and are therefore dependent on the varying normal strengths in the animals involved.

INJURIES OF THE LIGAMENTS OF THE KNEE JOINT

AN EXPERIMENTAL STUDY

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There has been substantial clinical proof in the past few years that the cruciate ligaments play a role secondary to that of the collateral ligaments in preservation of the stability and function of the knee joint. As I have noted in a previous communication,[1] several observers have shown that a torn anterior cruciate ligament may be disregarded or a fractured tibial spine and anterior cruciate ligament excised without marked impairment of the integrity of the knee joint, provided the collateral ligaments are intact. This fact has led some authors (Bennett,[2] Milch [3]) to undertake successfully the repair of the collateral ligaments alone, disregarding the associated tears of the cruciate ligament.

This concept, at variance with the teachings of most anatomists, was corroborated anatomically by me [4] after a study of the knee joints of human cadavers at the Daniel Baugh Institute of Anatomy in Philadelphia. The collateral ligaments were noted to be the structures most essential to preservation of the intrinsic stability of the extended knee, inhibiting lateral and rotatory motion of the tibia on the femur. In the absence of the cruciate ligaments, the internal lateral ligament, especially through its anterior portion, which remained taut in flexion, efficiently checked internal rotation, anteroposterior motion and distraction of the tibia from the femur in the flexed knee. Both cruciate ligaments, contrary to usual teachings, were most tense in flexion and internal rotation of the tibia on the femur. Their action was found to be accessory to that of the collateral ligaments and not indispensable to the stability of

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From the Department of Orthopedic Surgery, Jefferson Medical College.

1. Horwitz, M. T., and Davidson, A. J.: Newer Concepts in the Treatment of Injuries of the Ligaments of the Knee Joint: An Evaluation of the Mauck Operation, Surgery **3**:407, 1938.

2. Bennett, G. E.: Relaxed Knees and Torn Ligaments, Proc. Internat. Assemb. Inter-State Post-Grad. M. A., North America **6**:351, 1931.

3. Milch, H.: Injuries to the Crucial Ligaments, Arch. Surg. **30**:805 (May) 1935.

4. Horwitz, M. T.: An Investigation of the Surgical Anatomy of the Ligaments of the Knee Joint, Surg., Gynec. & Obst. **67**:287, 1938.

the knee joint. Experimental tears of the cruciate ligaments without associated fractures (except of the tibial spine) were best obtained in the human cadaver by forcibly abducting the tibia on the femur, with the knee and hip joints flexed and the pelvis fixed, and occurred only after the internal lateral ligament had also given way (Pringle [5]). The frequent association of injuries to the collateral and cruciate ligaments of the knee joint and often of the meniscuses as well has been observed clinically.

HEALING OF DEFECTS OF THE COLLATERAL AND CRUCIATE LIGAMENTS

It has been reported that acute tears of the cruciate ligaments, as in total dislocations of the knee joint, will be repaired by simple immobilization of the knee in full extension. In the light of the aforementioned anatomic findings and of the experimental evidence to follow, it is suggested that the restoration of stability to severely traumatized knee joints by such conservative methods is due rather to the repair of associated tears of the collateral ligaments.

METHODS OF INVESTIGATION AND RESULTS

Group 1.—In 8 rabbits under ether anesthesia, longitudinal incisions were made directly over the inner aspect of the left knee. The internal lateral ligament was exposed and was incised transversely through part of its thickness just above the joint line; the tear was completed and enlarged by forcible abduction of the tibia on the femur. In 2 instances, a ¼ inch (0.6 cm.) segment was excised from the internal lateral ligament. The skin was sutured with black silk, and in 4 instances the leg was immobilized in plaster bandage in fullest extension (about 150 degrees), while in the remaining instances no fixation was employed. The rabbits were killed at periods varying from two to twelve weeks.

Healing in various stages was noted in each specimen. When the defect was a simple incision and tear, the tendinous ends became adherent with coagulated plasma, while where large gaps were created by excising ¼ inch (0.6 cm.) of the internal lateral ligament, the interval became filled with coagulated blood and fibrin (fig. 1*A*). This was followed by replacement with soft fibrous tissue and then by formation of dense scar tissue, at first vascular and red and later white (fig. 1*B* and fig. 2*BE*). Histologically the process of repair was that normal to connective tissue (Boyd [6]), the primary scaffold of coagulated blood and fibrin being penetrated by proliferating young fibroblasts and vascular endothelial buds from the open tendinous ends and from the adjacent

5. Pringle, J. H.: Avulsion of the Spine of the Tibia, Ann. Surg. **46**:169, 1907.

6. Boyd, W.: A Textbook of Pathology, ed. 2, Philadelphia, Lea & Febiger, 1934.

Fig. 1.—*A*, internal lateral ligament of the left knee of a rabbit, two weeks after excision of ¼ inch (0.6 cm.) of the ligament. A hemorrhagic clot has filled the gap between the ligamentous ends. *B*, internal lateral ligament of the right knee of a rabbit, three weeks after excision of ¼ inch (0.6 cm.) of the ligament. The gap is completely bridged by vascular connective tissue. *C*, anterior cruciate ligament of the right knee of a rabbit two weeks after division. The ligamentous ends are ununited and retracted.

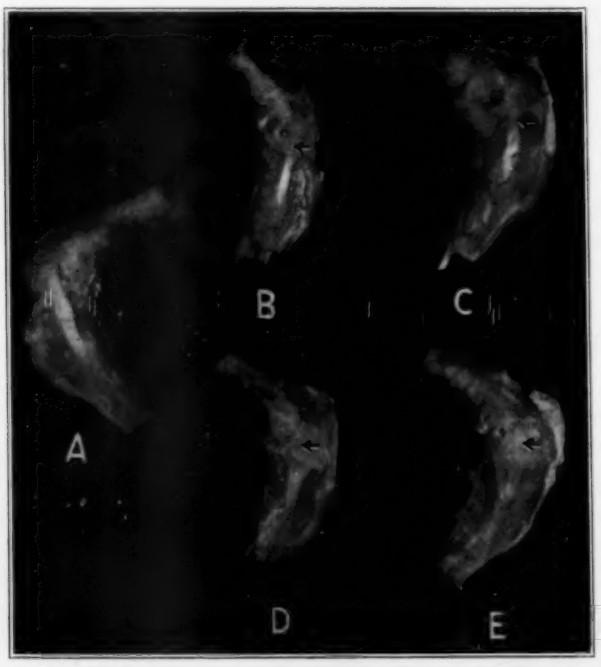

Fig. 2.—Internal lateral ligament. *A*, normal right knee (rabbit). *B* to *E*, left knees (rabbit six, eight, ten and twelve weeks respectively) after division of the ligament above the level of the joint line. Firm union is present in all specimens, the scar tissue being vascular and red in *B* and *C* and avascular and white in *D* and *E*.

tissues. At the end of three months the specialized connective tissue of the ligament had not completely replaced the scar tissue. This finding differs from the experience of Garlock,[7] who noted such complete substitution of the scar tissue in twenty-eight days after injury of the tendon.

Group 2.—In 8 rabbits under ether anesthesia, through a longitudinal incision between the patella and lateral femoral condyle of the right knee, the cruciate ligaments were severed with a tenotome, the anterior in 6 instances, the posterior in 1 and both in 1. The wound was closed with black silk and the extremity was encased in a plaster bandage with the knee at fullest extension (150 degrees). The rabbits were killed at periods varying from two to twelve weeks.

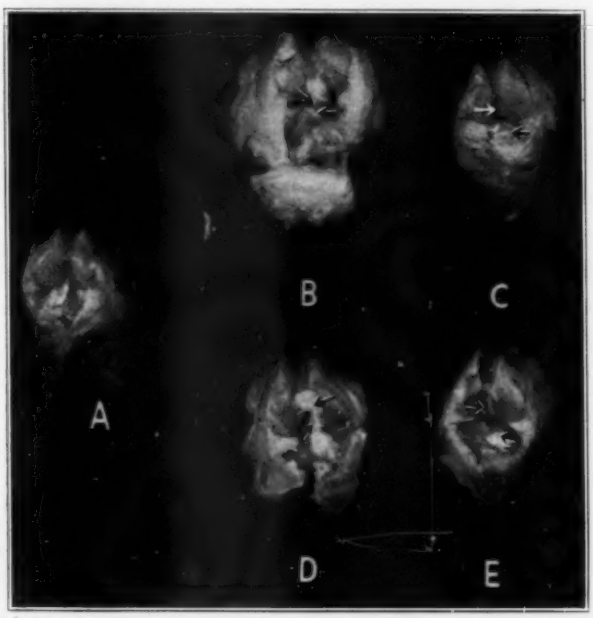

Fig. 3.—Cruciate ligaments. *A*, cruciate ligament of the normal left knee of a rabbit. *B*, *C*, *D* and *E*, right knees of rabbits, six, eight, ten and twelve weeks, respectively, after division of the anterior cruciate ligament in *B*, *C* and *E* and of the posterior in *D*. There is failure of union in all specimens, with retraction of the ligamentous ends in *B* and *D*, and gradual absorption of these stubs in *C* and *E*.

Union of the severed cruciate ligaments failed to occur in all specimens (fig. 1*C* and fig. 3*B*, *E*). In the early stages the joint was found filled with coagulated blood, fibrin and synovial fluid, and there was slight congestion of the synovial membrane and the infrapatellar

7. Garlock, J. H.: The Repair Processes in Wounds of Tendon and in Tendon Grafts, Ann. Surg. **85**:92, 1927.

fat pad. As early as two weeks after the operation much of the joint reaction had subsided, and the ends of the severed ligament were so retracted that they could no longer be approximated (fig. 1*C*). In the later specimens, these ligamentous ends became frayed, further retracted and gradually absorbed, so that ultimately only small stubs remained at the bony attachments (figs. 3*C* and 3*E*).

COMMENT

Union of the internal lateral ligament was firm in each instance as early as six weeks after the injury, with or without immobilization, and no preternatural mobility could be elicited. The opportunities for primary union of simple tears of this ligament are excellent, the small gap being immediately bridged by reparative elements. Where a large gap exists, healing is also satisfactory, for the interval is filled by localized hemorrhage and by the formation of richly vascular granulation tissue.

Several reasons are advanced, from this study, to explain the invariable occurrence of nonunion of cruciate ligaments in laboratory animals despite adequate fixation:

1. Hemorrhage does not remain localized between the severed ends of the ligament but is immediately dispersed within the joint cavity.

2. This blood is diluted by combination with synovial fluid, the formation of which is stimulated by the articular trauma and by the blood extravasation itself.

3. The ends of the severed ligament lie free within the joint cavity and are kept apart mechanically by the joint effusion.

4. The ligamentous ends retract early and tend to "curl up," and eventually they absorb so that only stubs remain at the bony attachments.

Histologic sections of the internal lateral ligaments of the knee joints of well preserved cadavers, prepared for my use by Dr. Andrew J. Ramsay, reveal that the collagenous fibers are arranged in parallel and compact bundles, while interposed are small areas of loose connective tissue containing isolated vessels; the Weigert elastic tissue stain reveals only an occasional elastic fibril (fig. 4*A*). The cruciate ligament is made up of aggregations of collagenous fibers less uniformly arranged, and interposed are large areas of loose connective tissue containing many vascular channels and an abundant network of elastic tissue (fig. 4*B*).

The tendency for the severed ends of the cruciate ligament to retract and the failure of those of the internal lateral ligament to do so are explained in great part by this variation in elastic tissue content. The deficient vascularity of the collateral ligament is compensated by the abundant supply of the adjacent subsynovial tissue (joint surface)

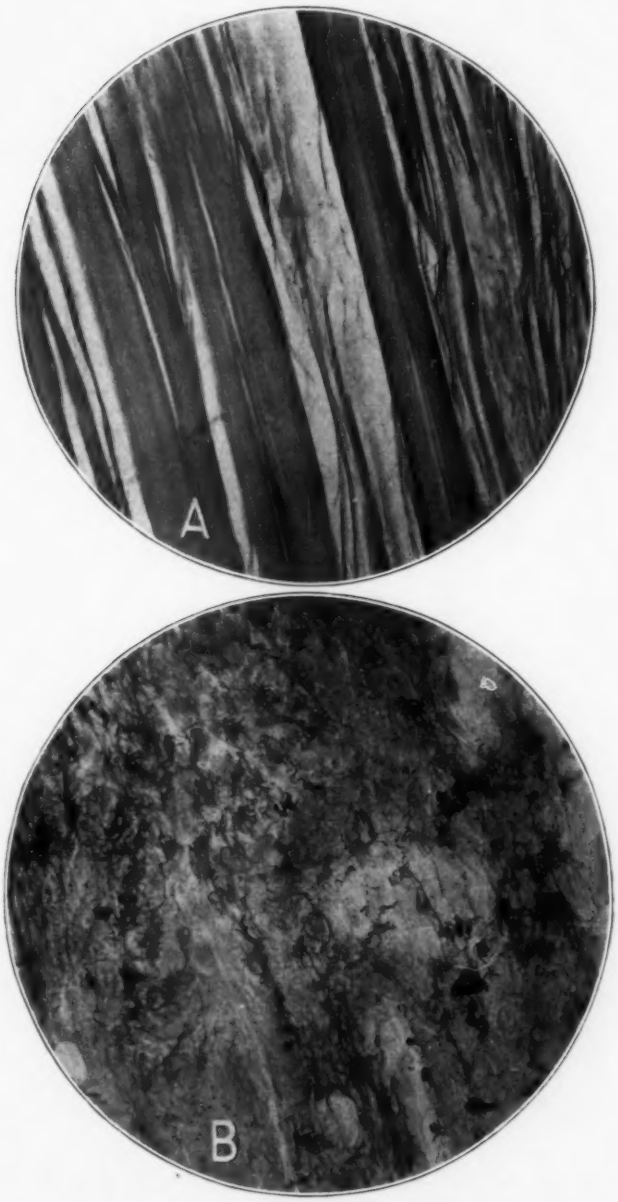

Fig. 4.—*A*, section of the human internal lateral ligament, × 100. The Weigert elastic stain was used. Note the regular arrangement of closely packed bundles of parallel collagenous fibers. Small amounts of loose connective tissue are interposed, but few elastic fibrils were located. *B*, section of the human anterior cruciate ligament, × 100. The Weigert elastic stain was used. Note the abundant loose connective tissue interposed between less uniformly arranged bundles of collagenous fibers (not shown), with an abundant fine elastic tissue network.

and by that of the overlying connective tissues. The blood supply of the cruciate ligament, although richer than that of the lateral ligament, is poorly supplemented by that of the subsynovial tissue, which only partly covers it.

SITE OF RUPTURE IN TEARS OF THE COLLATERAL AND CRUCIATE LIGAMENTS

Group 1.—Four human (cadaver) knees were stripped of their soft tissues and of their muscular and tendinous attachments. With the knee joint fully extended, the tibia was forcibly abducted on the femur until the internal lateral ligament was torn. This procedure was repeated, the hindlegs of two freshly killed rabbits being used.

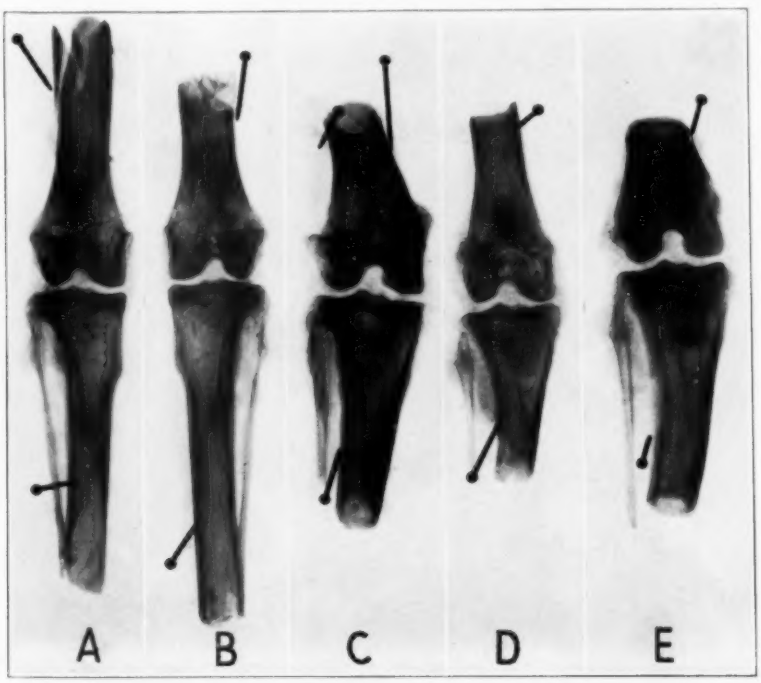

Fig. 5.—Roentgenograms of knees of rabbits, two weeks (*A* and *B*) to three months (*E*) after division of the internal lateral ligaments just above the level of the joint line. In no specimen is there evidence of pathologic calcification or ossification at the site of operation. The bony deposits at the femoral attachments of the ligament in specimens *A* and *B* probably represent small exostoses.

In each instance the internal lateral ligament was seen to tear close to its bony attachment, in 3 of the human and in 2 of the rabbit specimens at the femoral attachment and in 1 of the human and in 2 of the rabbit knees at the tibial insertion.

Group 2.—In four human (cadaver) knees, after division of the internal lateral ligament the anterior cruciate ligament was torn by acute abduction of the tibia on the femur with the knee and hip joints flexed and the pelvis fixed.

In each instance the cruciate ligament was torn close to its tibial attachment, and in 1 instance a portion of the tibial spine was also torn away.

COMMENT

These results are in keeping with the experimental findings of McMaster [8] relative to tendon and muscle ruptures. This author found that normal tendon did not rupture even when subjected to severe strain, but that the tendon insertion pulled away, the muscle tore in its belly or at its origin or fracture of the bony attachment at either end occurred.

Miltner [9] in his work on the experimental production of articular sprains in rabbits noted that when considerable force was employed, in addition to synovial, subsynovial and articular changes, there was microscopic evidence "of a tearing injury at the point of insertion of the ligaments into the bone. Small bits of bone had been torn loose and tended to grow in the new location."

In Pellegrini-Stieda [10] disease, a delayed calcification or ossification of the internal lateral ligament appears as a semilunar shadow on the roentgenogram several weeks after an injury to the knee. It is usually adjacent, but distinctly separate from the medial femorocondylar angle, although Finder [11] has observed the process in other parts of the internal lateral ligament. Regardless of the various theories of origin, the vulnerability of the internal lateral ligament near its femoral attachment is once more apparent. The absence, roentgenographically, of pathologic calcification or ossification in those rabbit specimens in which the internal lateral ligament had been traumatized (fig. 5) may be considered evidence against the metaplastic theory and in favor of the belief that the process in Pellegrini-Stieda disease represents either a true, detached fracture of a spicule of bone or a fractureless callus formation due to periosteal tear.

The lateral and cruciate ligaments, like tendons, are therefore weakest and most susceptible to trauma at their osseous attachments, and one may anticipate, in the presence of adequate injury, the occurrence

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8. McMaster, P. E.: Tendon and Muscle Ruptures, J. Bone & Joint Surg. **15**: 705, 1933.

9. Miltner, L. J.; Hu, C. H., and Fang, H. C.: Experimental Joint Sprain: Pathologic Study, Arch. Surg. **35**:234 (Aug.) 1937.

10. Stieda, A.: Ueber eine typische Verletzung am unteren Femurende, Arch. f. klin. Chir. **85**:815, 1908.

11. Finder, J. G.: Calcification of the Tibial Collateral Ligament: A Report of Forty-Two Cases, J. A. M. A. **102**:1373 (April 28) 1934.

of tears of the ligaments at these sites or even actual fractures of the bony insertions themselves, e. g., paracondyloid fracture of the femur or tibia or fracture of the tibial spine.

CONCLUSIONS

Although the following conclusions are derived from a study of knee joints in rabbits and in human cadavers, their application to the living human being is substantiated by clinical experiences and observations.

1. In rabbits, tears of the internal lateral ligament of the knee joint repair regardless of the size of the defect and whether or not fixation is employed. Tears of the cruciate ligaments do not repair by such simple fixation, and the severed ends can be approximated surgically only in the early stages after injury. It is suggested, in the light of anatomic studies which have revealed the primary importance of the internal lateral ligament to the stability and function of the knee joint, that the satisfactory results obtained by conservative fixation in human patients with tears of the cruciate ligament are due in reality to repair of associated injuries to the collateral ligament.

2. The ligaments of the knee joint in human cadavers and in freshly killed rabbits are weakest at or near their bony attachments, and these sites, in the presence of adequate trauma, are liable to varying degrees of tear or fracture.

RESULTS OF TREATMENT OF CHRONIC INDOLENT WOUNDS WITH AZOCHLORAMID

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Wounds involving the skin and the subcutaneous tissues are readily attacked by pyogenic organisms. In the majority of cases the superficial nature of the wound, which permits adequate drainage, results in satisfactory healing. A certain percentage of such wounds, however, become chronically infected because of some complicating factor, such as diabetes, a circulatory disturbance or trauma resulting in devitalization of the surrounding tissues. The protracted course of infected wounds in diabetic patients despite adequate diabetic therapy, the tenacious infections in wounds following the excision of carbuncles and the chronic sloughing wounds following subcutaneous trauma often discourage both patients and surgeons. The use of compresses wet with hot saline solution is beneficial in such cases, but the method is laborious and sometimes fails to clean up the infection. The present study was undertaken to determine whether a simpler and more effective method of treatment could be found, which would result in reducing the time and effort required to promote primary healing or to prepare such a wound for secondary surgical closure or grafting.

My attention was attracted to azochloramid, a new complex chlorine compound which liberates small amounts of chlorine gradually over a long period. This is in contrast with the rapid liberation of chlorine from Dakin's solution, which requires frequent changes of dressing and precautions against irritation.

In the present series of cases a stable oily solution, azochloramid in triacetin (1:500) was used in the following manner: Sterile sponges were soaked in this solution and applied directly to the wound. The saturated sponge was overlaid by a pad of abdominal gauze, and a sheet of rubberized silk or other impervious material was placed over this. Retention of the oily azochloramid solution on the wound surface was thus insured, and the dressing separated easily from the tender granulations. The dressings were changed twice daily by the nurse, who used a technic similar to that employed with hot sterile saline compresses. In the presence of spreading infections for which heat also is indicated, hot

From the surgical pathologic laboratory of the Department of Surgery, the Johns Hopkins Hospital and University.

sterile saline compresses are placed over the azochloramid sponges and the sheet of rubberized silk placed over the compresses.

While azochloramid may be of value as a dressing for several types of cutaneous wounds, it seems of special value in the treatment of large necrotic lesions. The best results have been obtained in cleaning up large granulating wounds and promoting growth of healthy granulation tissue either for secondary closure or for skin grafting. It is important to emphasize that this antiseptic does not take the place of careful surgical procedures and hot saline compresses when heat is indicated, as for an acute infection which is not localized.

In several cases of chronic infection which did not respond satisfactorily to other therapy, the application of azochloramid rapidly brought about improvement and shortened the time necessary before skin grafting or secondary closure.

The cases to be reported have been divided into three groups. Group 1 consists of 3 cases of chronic infection which did not respond satisfactorily to other forms of therapy; group 2 consists of 3 cases in which large, necrotic granulating wounds remained after excision of carbuncles, and group 3 consists of 2 cases of severe cutaneous flesh wounds with subsequent necrosis of the skin and superficial muscles in children. All of the cases have been followed carefully in the hospital, with pictures, cultures and frequent examinations to note the course.

GROUP 1

CASE 1.—A white man aged 58, of Italian descent, was admitted to the hospital on Feb. 17, 1938, with varicose veins and a large, foul ulcer of the leg. He had been coming to this hospital for fourteen years because of a chronic ulcer of the left leg. Ligations and injections of numerous veins and various types of dressings had been employed during this period, but the ulcer had persisted and had become larger. The patient had persistently refused to cooperate by keeping off his feet and had once refused admission to the City Hospital after all arrangements had been made. On the present admission he did not appear ill, but a large, very foul ulceration covered a large area of the lower part of the left leg, from the ankle to the knee, on the anterior and medial aspects. The edges of the ulcer were rolled up and bluish. The surrounding skin was scarred and brown. The ankle and foot distal to the ulcer showed a thickened scar encircling the ankle. There was considerable peripheral edema. Proximally there were fairly extensive varicose veins, with a few smaller ones on the right leg (fig. 1).

The patient was kept in bed with the leg elevated. Hot sterile saline compresses, changed regularly (every two hours by day and every four hours by night), were applied to the ulceration. Roentgenograms revealed some evidence of osteomyelitis and extensive periostitis of the tibia and fibula of the left leg. The nonprotein nitrogen content and the sugar content of the blood were normal. There was little response to this therapy, the wound remaining necrotic, with poor granulations. The odor was so foul that the patient was isolated in a private room. A 1:500 solution of azochloramid in triacetin was then applied four times a day, soaked in

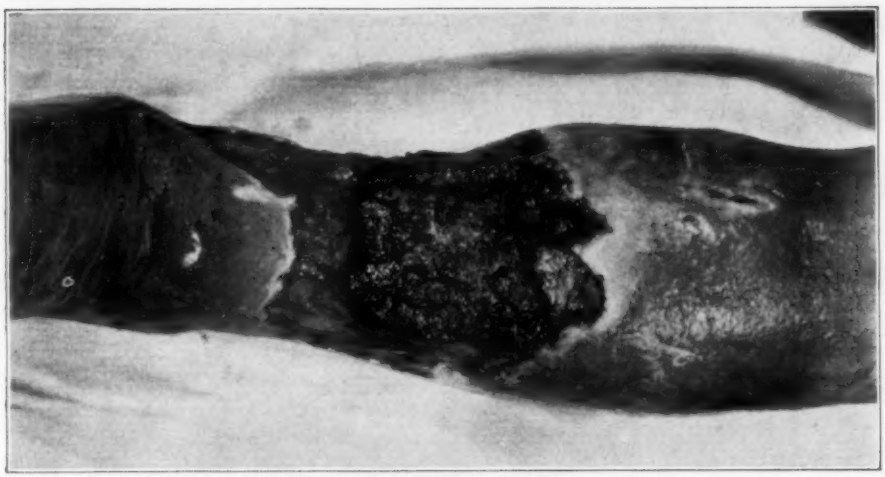

Fig. 1.—Indolent ulcer of the leg of many years' duration in a white man aged 58. He had had varicose veins for fourteen years. The Wassermann reaction was negative. Note the necrotic granulation tissue and the edema of the surrounding skin.

Fig. 2.—Same wound as in figure 1, twenty-four days later, after débridement and skin grafting.

sterile sponges. Within three days the odor had practically disappeared, and the granulations were cleaner. Within a week there was improvement in the cleanliness of the wound, although there was no regeneration of epithelium. In twelve days the cultures, which had shown a heavy growth of Bacillus proteus before azochloramid therapy was started, were sterile. The use of azochloramid was continued over a total period of twenty-one days. During this time the entire ulceration (15 by 15 cm.) acquired red, healthy granulation tissue, but there was little epithelization. The surrounding indolent skin was then debrided, and hot sterile saline compresses were applied for several days, after which a series of pinch grafts were applied at several subsequent operations, the majority of the grafts "taking" nicely (fig. 2).

Fig. 3.—Infected amputation wound of the left thigh in a 72 year old white woman with diabetes, arteriosclerosis and gangrene of the left foot. Little response was shown to daily washing with alcohol, to dry dressings or to adhesive traction.

Case 2.—A 72 year old white woman had had diabetes for fifteen years. She was admitted to the hospital on Feb. 22, 1937, because of gangrene of the left great toe of six months' duration. The Wassermann reaction was negative. Despite all conservative measures there was no improvement in the gangrene, which progressed slowly and produced more pain. A Gritti-Stokes amputation at the knee was performed. Healing was satisfactory for one week, but infection of the stump developed, and on the tenth postoperative day the wound broke open, with wide gaping of the edges of the skin. There was no response to the use of alcohol and daily dressings with adhesive skin traction. Azochloramid in triacetin (1:500) was started, and the dressings were changed twice daily. Healthy granulation tissue soon developed, and after thirteen days the wound was clean. A secondary closure was then successfully performed (fig. 3).

Case 3.—A white woman aged 41 was admitted to the hospital on March 2, 1938, because of a tremendous ventral hernia with ulceration of the overlying skin (fig. 4). The hernia had been present for seven years, starting as a small umbilical hernia and increasing rapidly in size since her eighth pregnancy, with

ulceration of the skin two months before the present admission. Hot saline compresses were applied to the ulcerations to clean them up before a hernia repair could be performed. There was little improvement in the ulcerations after one week of continuous treatment, so a 1:500 solution of azochloramid in triacetin was tried. There was prompt improvement in the chronic ulcerations, which decreased in diameter from 2 to 3 cm. to 1 cm. during the eight days in which azochloramid was applied. The ulcerations were exposed to the air after the azochloramid was discontinued, and scarlet red was applied to stimulate epithelial growth. The ulcerations were completely healed at the end of ten days. Herniorrhaphy was then successfully performed, the wound healing by first intention.

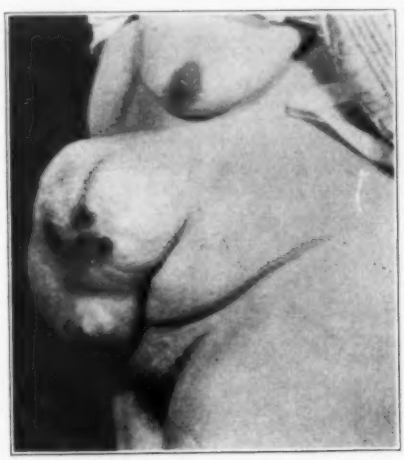

Fig. 4.—Large ventral hernia with ulcerations of the skin in a 41 year old white woman. The ulcerations did not respond to hot sterile compresses.

GROUP 2

CASE 1.—A white man aged 59 was admitted to the hospital April 15, 1937. He was acutely ill, with signs of severe diabetes and a large carbuncle with a surrounding area of cellulitis involving the left shoulder. The sugar content of the blood on admission was 393 mg. per hundred cubic centimeters, and a test for acetone in the urine gave a 4 plus reaction. The Wassermann reaction was negative. Culture of the blood yielded bacteria, numerous colonies of Staphylococcus aureus being obtained. The patient received active treatment for the diabetes and septicemia. The shoulder was compressed with hot saline compresses for five days, after which the carbuncle was excised (fig. 5). Cultures revealed Staph. aureus from the carbuncle. Azochloramid in triacetin (1:500) was applied to the crater twice daily, hot sterile saline compresses being applied over the azochloramid sponges. The wound at the onset of treatment was dirty and necrotic, but despite the stormy course (five cultures of the blood yielded staphylococci) the wound began to show healthy granulation tissue. The surrounding cellulitis subsided, and after twenty-five days of treatment with azochloramid secondary closure of the wound was successfully done. During this time frequent cultures were made of material from the wound, which showed progressive diminution in the number of colonies of Staph. aureus.

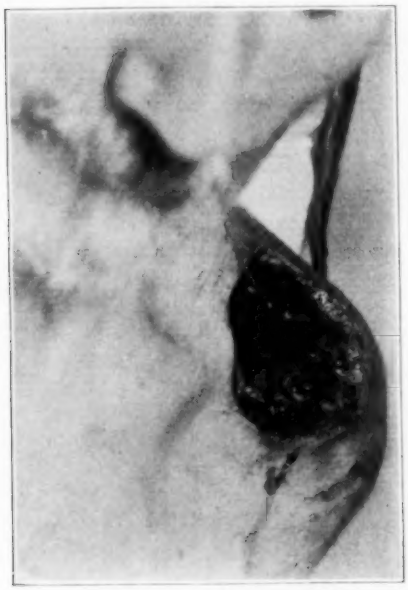

Fig. 5.—Necrotic wound after excision of a carbuncle of the left shoulder in a 59 year old white man who was acutely ill with staphylococcic septicemia and severe diabetes.

Fig. 6.—Condition in a white woman aged 52, with diabetes, after excision of a carbuncle of the right interscapular region. Note crusting and unhealthy appearance of the base of the wound after eight days' treatment with hot sterile saline compresses.

CASE 2.—A white woman aged 52 was admitted to the hospital March 31, 1937, with a diagnosis of diabetes mellitus and a large carbuncle on her back. The diabetes was easily controlled, and hot saline compresses were applied to the carbuncle. After eight days the carbuncle was thought to be sufficiently localized for excision. This was done successfully, Staph. aureus being cultured from the wound. The crater was 7 cm. in diameter (fig. 6). Healing was delayed, and after eight days azochloramid in triacetin (1:500) was tried in an endeavor to speed up the healing of the wound. After four days of therapy with azochloramid and hot sterile saline compresses there was a marked improvement in the appearance of the wound. Red granulation tissue grew rapidly, decreasing the depth of the crater. Fourteen days after the azochloramid treatments were begun the wound was grafted with small pinch grafts, which "took" satisfactorily.

Fig. 7.—Large deep wound after excision of a carbuncle of the neck in a 54 year old white man. Spreading of this wound occurred, so that a second incision was necessary. Azochloramid was subsequently discontinued.

CASE 3.—A white man aged 54 was admitted to the hospital March 5, 1938, with a large carbuncle on the back of his neck, of two weeks' duration. The carbuncle was compressed for two days before surgical excision was performed (fig. 7). Cultures revealed Staph. aureus. Azochloramid in triacetin (1:500) was applied on the second day after the operation. Hot sterile saline compresses were applied over the azochloramid sponges. The wound did not respond satisfactorily, for the carbuncle spread to the opposite side of the neck. Accordingly, a second excision of the area of spread was necessary one week later. The diameter of the crater was now 9 cm. and its depth 1.5 cm. Azochloramid was again applied, but after two days the patient complained of such pain and irrita-

tion of the wound when it was applied that the azochloramid was discontinued. At the time of writing the wound is healing slowly with hot sterile saline compresses.

GROUP 3

CASE 1.—A white boy aged 1½ years caught his left arm in a washing machine wringer, traumatizing the subcutaneous tissues. The skin and bones were not

Fig. 8.—Sloughing wound of the left forearm of a 1½ year old child whose arm was caught in a washing machine wringer. Note the surrounding inflammation of the skin.

Fig. 9.—Wound similar to that in figure 8 in a 3½ year old Negro boy. There was also a surrounding area of induration and inflammation, which caused this wound to respond better to hot sterile saline compresses than to azochloramid.

injured. The boy was admitted to the hospital for observation on Feb. 19, 1938, and several days later the subcutaneous tissues and skin in the anticubital fossa began to slough. A foul, necrotic sloughing area about 5 cm. in diameter developed

(fig. 8). Culture revealed an alpha streptococcus. Azochloramid in triacetin (1:500) was applied on gauze sponges twice a day. The wound began to look more healthy, but repair was sluggish. After eight days, treatment with azochloramid was discontinued, and the use of hot sterile saline compresses was instituted, with slightly more rapid improvement. Grafts were applied to the area about a week later, but only approximately half of them "took"; hence secondary closure was necessary ten days later.

CASE 2.—A Negro boy aged 3½ years was admitted to the hospital on March 2, 1938, for observation, with an injury similar to that in the foregoing case. He had caught his arm in a washing machine wringer, injuring the soft parts but not the bone. While he was in the ward, an area about 5 cm. in diameter over the brachioradialis muscle began to slough. Application of hot sterile saline compresses were begun, but after two days it was discontinued and azochloramid in triacetin (1:500) started. The repair of the wound was slow, and after eight days' treatment the azochloramid was discontinued and the use of hot sterile saline compresses again started. The improvement under the latter therapy the second time was definite, which illustrates the point that azochloramid will not act as a substitute for local heat in the treatment of wound infections which are not sufficiently localized (fig. 9).

SUMMARY

Eight large, necrotic infected wounds have been treated with azochloramid in triacetin (1:500). The wounds selected have been indolent in character, most of them complicated by other factors, such as diabetes or vascular disease. Six of the 8 presented localized infection, 2 infections being in a less localized stage.

A satisfactory response was obtained in 5 of the 6 cases. The character of the granulation tissue changed after a few days from sluggish, gray granulations into a rapidly growing bed of red granulation tissue of healthy appearance.

In the sixth case there were signs of irritation on the second day, and the solution was discontinued.

In the other 2 cases the infections were not sufficiently localized, and hot saline compresses seemed of greater value.

In conclusion, it may be stated that azochloramid (1:500 solution in triacetin) is an antiseptic which appears to be of value in the treatment of chronic infections of the indolent type described. Sterile sponges soaked in this solution, changed twice or four times daily, exert a continuous antiseptic action and require a minimum of attention. The solution promoted development of healthy granulation tissue, or primary healing, in a group of infected wounds for which other types of therapy previously tried had offered little or no benefit.

SIXTY-EIGHTH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY

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CONGENITAL DEFORMITIES

Madelung's Deformity.—Anton and his associates [1] review 171 cases of Madelung's deformity collected from the literature and add 1 case of their own. They find that this deformity may involve any or all of the structures about the wrist. It is essentially, however, a defect of the lower end of the radius, an osteochondritic dysplasia with palmar bowing of the distal end of the radius. Posterior subluxation of the lower end of the ulna, always present, is more apparent than real. In the more severe forms there may be overriding of the ulna on the carpal bones. In 127 of the 171 cases reviewed, the deformity was bilateral. Heredity seemed to play a part in the development of the lesion in one third of the cases. The patients commonly had pain during the growing years, which ceased when growth in the radius ended. The authors advise palliative treatment until growth is attained, after which the most satisfactory treatment, they believe, is osteotomy of the lower end of the radius with correction of the bowing and shortening of the ulna if necessary.

This report of progress is based on a review of 198 articles selected from 334 relating to orthopedic surgery and appearing in the medical literature approximately between July 1 and Nov. 1, 1938.

1. Anton, J. I.; Reitz, G. B., and Spiegel, M. B.: Ann. Surg. **108**:411, 1938.

Congenital Anomalies of the Spine.—Bailey and Carter [2] in a study of spinal anomalies attempt to correlate the anatomic, roentgenologic and clinical findings. They find that anomalies occur in 67 per cent of spines. They discuss the development of fused vertebrae, hemivertebra, spina bifida, transitional vertebrae, spondylolisthesis and persistent epiphysis of the vertebral process. The latter anomaly is sometimes of medicolegal importance. It can be differentiated from a fracture by the following observations: 1. The epiphysis is separated from the other portion of the vertebra by cartilage. 2. There is absence of compression of the vertebral body. 3. There is no offset of the fragment. 4. It does not change place with motions of the spine.

Early Treatment of Congenital Dislocation of the Hip.—Emphasizing the necessity for early diagnosis and treatment of congenital dislocation of the hip, Kickehayn [3] reviews the material collected between 1930 and 1935 at three large German clinics. During this period 39 dislocations were reduced during the first year of life, 117 in the second and 56 in the third. There was no recurrence of dislocation in the first year group; there were 6.8 per cent recurrences in the second year group and 7.1 per cent in the third year group. Often the oblique acetabular roof of the dislocated hip became a normal roof. This observation was frequent in cases of dislocation reduced during the first year. Rapid acetabular development was also shown during treatment in the preluxated type. In the cases reported the children were fitted with abduction splints after approximately seven weeks in plaster. The author feels that in the preluxation stage the abduction treatment offers at present the best prospects. The available statistics are scanty and for the most part are too recent to permit of any assurance. He cites a fifteen year follow-up by Elsner on a hip reduced at 5 months. The result was faultless.

Aberle [4] reports 4 cases of hallux varus of congenital origin, adding them to the 70 cases already reported in the literature. This deformity of the first metatarsal bone and phalanges is characterized also by marked broadening of the component bones of the first toe. This broadening is a consequence of congenital duplication of the "big toe ray." All variations, from separate to fused duplicate bones, have been reported. One patient presented, in addition to congenital varus, unusual shortening and broadening of the tibias as well as bilateral congenital dislocation of the fibulas at the knees. Correction is often necessary to permit the wearing of a shoe. The author prefers to resect the base of the proximal phalanx or to combine this resection with resection of the head of the first meta-

2. Bailey, W., and Carter, R. A.: California & West. Med. **49**:46, 1938.
3. Kickehayn, R.: Ztschr. f. Orthop. **67**:245, 1938.
4. Aberle, W.: Ztschr. f. Orthop. **67**:165, 1938.

tarsal bone. This gives adequate relaxation of the contracted phalanx. He advises that incisions be placed laterally rather than medially.

DEVELOPMENTAL DISEASES OF BONE

Coxa Plana Following Severe Trauma.—Nielson [5] reports 2 cases of coxa plana subsequent to fracture of the neck of the femur, in boys. He postulates an injury to the nerves of the afferent blood vessels. The resultant impairment of nutrition leads to osseous and cartilaginous changes. In the opinion of the author, the severity of the lesion is dependent on the degree of impairment of the circulation.

First Stages of Coxa Plana.—Waldenstrom [6] states that in the very earliest stage of coxa plana the change shown in the anatomic specimen is primary necrosis followed by resorption of the necrotic cancellous tissue and later by formation of new bone and cartilage. Of the patients who have been personally treated by him during the past thirty years, 13 came under his observation at this early stage of the disease. The first symptom of the disease was a limp, sometimes associated with pain in the hip. Also, there was restriction of mobility which when compared with that of the sound hip could be expressed in degrees. Four patients consulted the author when limping had been present for only a few weeks. An anteroposterior roentgenogram taken at that time was normal. Unfortunately, a lateral view was not taken. The author feels that a lateral view always shows the deformity more definitely. Two or three months after the start of limping the characteristic signs of coxa plana appeared; i. e., the normal cancellous tissue in the upper part of the epiphysis began to show on the articular surfaces the effects of resorption. The roentgenograms in these cases of incipient coxa plana showed one constant change in the diseased hip joint, an increase in the distance between the epiphysis and the bottom of the acetabulum. The article is well illustrated by roentgenograms.

TUBERCULOSIS

Fusion of the Spine.—Swift [7] tabulates the end results of the fusion operation for tuberculosis of the spine in 309 children 10 years old or younger. All of these children were operated on at the New York Orthopaedic Dispensary and Hospital between 1911 and 1932. Seventy-four per cent were found to be leading a normal life without recurrence of the disease. Fifteen per cent had pseudarthroses which required further operations. In 11 per cent the results were poor. Fifteen per cent of the children have died. Two children died of the operation.

5. Nielson, B.: Hospitalstid. **81**:773, 1938.
6. Waldenstrom, H.: J. Bone & Joint Surg. **20**:559, 1938.
7. Swift, W. E.: J. Pediat. **13**:248, 1938.

POLIOMYELITIS

Studies of Poliomyelitis.—Brodie [8] states that neither the portal of entry nor the pathogenesis of poliomyelitis has been finally determined in the human being. Therefore too close an analogy between the experimental and the human disease cannot be drawn. He concludes that there is evidence that more than one strain of virus exists. Neither convalescent serum nor any of the other means of treatment available offers hope for the prevention or limitation of paralysis. The value of active immunity as a preventive is still undetermined. Nasal sprays are effective in protecting monkeys, but in human beings the results from the use of these sprays are not encouraging.

OSTEOMYELITIS

Subacute Infection of Bone.—Kuth [9] reports 4 cases of subacute infection of bone, or osteoperiostitis albuminosa Ollier, and gives an excellent review of the subject. This infection is caused by a pathogenic organism of low virulence. The lesions are mild and benign and respond to simple incision with adequate drainage and removal of sequestrums. The article is well illustrated.

CHRONIC ARTHRITIS

Treatment of Rheumatoid Arthritis with Large Doses of Vitamin D.—Abrams and Bauer [10] observed the effects of massive doses of vitamin D on 18 patients with rheumatoid arthritis over periods of from four to thirteen months. Prior to treatment all the patients were in a state of stationary or slowly progressive illness. Subjective improvement was observed during treatment in 8 patients. In only 3 patients was objective improvement observed and in only 1 was it marked. Other observations were equally disappointing. The conclusion was that massive doses of vitamin D are of little value in altering the course of the disease. The effects of the large doses did not differ from those of the usual therapeutic doses and did not justify the expense and danger involved.

Osteoarthritis Cretinosa.—Ludwig [11] suggests that the changes found in the bones and joints of cretins be named "osteoarthritis cretinosa." In only 2 of 49 adult cretins were the hips normal in roentgenologic examination. The abnormalities noted were flattening and broadening of the

8. Brodie, M.: Am. J. Pub. Health **28**:746, 1938.

9. Kuth, J. R.: Subacute Infections of Bone: Osteoperiostitis Albuminosa Ollier, Arch. Surg. **37**:46 (July) 1938.

10. Abrams, N. R., and Bauer, W.: The Treatment of Rheumatoid Arthritis with Large Doses of Vitamin D, J. A. M. A. **111**:1632 (Oct. 29) 1938.

11. Ludwig, H.: Fortschr. a. d. Geb. d. Röntgenstrahlen **57**:506, 1938.

femoral head, shortening of the neck, enlargement of the trochanters and irregular calcification. When the process was advanced there were arthritic changes, including free joint bodies. In the hips of children, irregularity in ossification was found. The picture simulated Legg-Perthes disease.

[EDITORIAL NOTE.—One of the editors has observed roentgenograms of cretins which show a picture similar to that of coxa plana. In cretins this condition is always bilateral.]

Postural Education.—Posture: Malcolmson [12] reviews the experience of the United States Naval Academy in postural training since 1921, when such training was introduced as a part of the physical examination of cadets. He gives five rules for postural training: 1. Stand with the heels together and the toes at an angle of 45 degrees. 2. Contract the buttocks slightly. 3. Clasp the forefingers lightly together behind the buttocks. 4. Raise the chest. 5. Release the hands and let gravity determine their position. Special instruction is given for the correction of local defects as shown in silhouette pictures. Malcolmson states that postural training should be started in early childhood; in this way many structural lesions would be prevented. He deplores the lack of agreement in definitions of good posture and feels that a generally acceptable concept would be reached if there were more studies of posture.

[EDITORIAL NOTE.—While there is lack of unanimity in defining good posture, there is fairly general agreement as to the end to be attained—a physically efficient body. There is, however, wide disagreement as to methods, which vary from supine relaxation to strenuous and rigid exercises. No method brings rapid correction. Probably with more attention to the carriage of the body in early childhood the tedious correction of faulty posture at a later age would not be necessary.]

BACK

Treatment of Scoliosis by Osseous Traction.—Goodwin and Althaus [13] make a preliminary report on traction applied directly on the spine for the correction of scoliosis. This was carried out in 2 cases after moderate correction had been obtained with the Risser jacket. Immediately after an operation for spinal fusion had been performed, stainless steel wires were applied about the spinous processes of the vertebrae in the compensatory curves and were then threaded under the muscles to the side of the body. The wires were made taut over a nail on the outside of the plaster cast. The wires were well tolerated, and much additional correction was obtained. In neither of the cases has

12. Malcolmson, J. E.: Arch. Phys. Therapy **19**: 348, 1938.
13. Goodwin, F., and Althaus, J. W.: Southwest. Med. **22**:253, 1938.

sufficient time elapsed to permit one to see whether the added correction will be permanent.

Treatment of Scoliosis by Means of the Wedging Jacket and Spinal Fusion.—Two hundred and sixty-five cases of scoliosis treated by the use of a wedging jacket and spinal fusion are reported by Smith, Butte and Ferguson.[14] In the eight year period covered by this study, 1,498 new cases of scoliosis were observed in the clinic of the New York Orthopaedic Dispensary and Hospital. In only 297, or 19 per cent, was operation performed. The indications for correction and fusion are: (1) a curve which is progressing in a growing child; (2) a severe curve with imbalance of the trunk, whether or not the patient is beyond the period of growth and (3) a deformity which is causing pain or fatigue. In some of the cases reported an operation was performed without previous correction. Some of the patients were given postural treatment. Three of these showed measurable improvement after corrective exercises. The jacket used is essentially the same as that first used by Risser in 1927 and described by him in 1931, the only modification being that the head is held in position toward the side of the concavity of the curve, to prevent undue stretching of the brachial plexus. This position, however, is not held forcibly to produce correction, as was previously advocated. The hinges are now placed more eccentrically, toward the convexity of the curve. In addition to straightening the primary curve, the wedging jacket simultaneously increases the compensatory curve. This change in the secondary curve is observed only while the patient is in the jacket. After the jacket is removed, the compensatory curve should straighten in proportion to the straightening obtained in the primary curve. The primary curve is determined by the criteria described by Ferguson: 1. In the case of three curves, the middle one usually is the primary curve. 2. The greater curve, or the one toward which the trunk is shifted, usually is the primary curve. 3. When in the sitting position the pelvis is elevated on the side of the convexity of the lumbar curve; this curve if it is compensatory will tend to straighten but if it is primary it will not. The operation is performed with the patient in the jacket. If the primary curve has been straightened completely, the fusion is limited to the vertebrae included in it. It is important that the end vertebrae should not be overcorrected; this may occur in a mild flexible curve. When correction is not complete, it may be advisable to extend the fusion beyond the limits of the primary curve. The object should be to extend the fusion to the part where the upper surface of the upper vertebra will be parallel to the lower surface of the lower vertebra. These surfaces should be at right angles to a line joining their centers. The time required for correction of the curve, including the application

14. Smith, A. DeF.; Butte, F. L., and Ferguson, A. B.: J. Bone & Joint Surg. **20**:825, 1938.

of the jacket and preparation for the operation, is from three to four weeks. Hibb's method of fusion is used in all cases. If four or more vertebrae are included in the fusion, the operation is done in two or more stages. This minimizes the occurrence of shock. The patient remains in the original jacket for three months after the last operation and during this time is kept in bed. The jacket is then removed, and a so-called semibent jacket is applied. It is put on with the patient lying supine on a strip of canvas. No attempt is made to straighten the back more than occurs naturally. A strip of plaster is included over the shoulder opposite the curve in order to hold the head and neck. The patient is now permitted to be up. At the end of three months the jacket is again changed and the shoulder strap is omitted. When this jacket is put on, the spine usually has nearly, but not completely, become straight. This jacket is removed in three months, and a roentgenogram is taken. If the fusion is continuous and mature, no other plaster is applied. No jacket, therefore, remains on longer than nine months unless the size of the patient or the appearance of the fusion in the roentgenogram makes it necessary to alter this rule. Pseudarthrosis occurred in the area of fusion in 61, or 23 per cent, of the 265 patients. Forty-seven of these patients were operated on again and the defect repaired. This pseudarthrosis occurred in the thoracolumbar region in 36 of the 61 cases. This indicates that particular care should be taken to produce strong fusion in this area. The results of the treatment were excellent or good in 79.7 per cent, fair in 15.6 per cent and poor in 4.7 per cent of cases.

[EDITORIAL NOTE.—Scoliosis remains one of the most difficult problems in orthopedic surgery. Admitted that the ideal treatment would be the prevention of scoliosis for the most part by corrective exercises for early muscular imbalance and the use of minimal supportive apparatus to maintain normal spinal contour, most patients seek treatment when such preventive measures are no longer possible. The careful work of this clinic has added greatly to knowledge of the mechanics and treatment of scoliosis.]

MUSCULAR DISTURBANCES

Isolated Paralysis of the Serratus Anterior Muscle.—So-called winged scapulas attributable to paralysis of the serratus anterior muscle were first described in 1825 by Velpeau. Since that time 150 cases have been reported, in most of which the condition was considered to be due to injury or disease of the long thoracic nerve rather than to laceration of the muscle itself. Horwitz and Tocantins[15] report 6 cases. The pathogenesis and kinesiologic observations are considered. Treatment

15. Horwitz, M., and Tocantins, L. M.: J. Bone & Joint Surg. **20**:720, 1938.

consists in relaxation of the paralyzed serratus anterior muscle and correction of the associated stretched and contracted muscles. The authors claim that this is effectively performed by a brace which they have illustrated. This brace eliminates both the winging and the abnormal rotation of the scapula. The authors recommend this apparatus also for the treatment of neuritis of the brachial plexus as well as cervical rib or scalenus anterior syndrome. The brace consists of a celluloid elbow, or cup, into which the point of the elbow fits snugly. It is held in place by an adjustable steel upright which rests on a chest band, a pelvic band and an iliac crest seat.

Scalenus Anterior Muscle in Relation to Pain in the Arm and Shoulder.—In addition to the scalenus anterior syndrome, which Ochsner and his associates [16] describe as characterized by pain referred to the shoulder, to the supraclavicular area, down the arm to the ulnar and flexor surfaces of the forearm, to the hand and frequently to the side of the neck and ear, Freiberg [17] finds that the pain is also present in an area between the spine and the mesial border of the scapula. Also, if the head is turned toward the affected side with the neck extended, on deep inspiration or on depression of the shoulder the pain is increased. The vascular manifestations consist of diminished pulse volume on the affected side, decreased temperature of the cutaneous surface, dulness, coldness and formication. These vascular changes can be proved by oscillometric tests. In cases in which the sternal end of the shoulder girdle presents arrested descent or in which the acromioclavicular descent is increased, symptoms develop. The author points out that lesions of the cervical portion of the spine as well as traumatic and infectious lesions of the shoulder girdle may be accompanied by the scalenus anterior syndrome but that section of the scalenus anterior muscle may not be necessary. When cervical lesions or lesions of the shoulder girdle are amenable to conservative therapy, such as improvement of general posture, rest in bed, traction on the forearm and upper part of the arm and wearing of braces, indiscriminate scaleniotomy is contraindicated. On the other hand, when there is anatomic malformation or when symptoms have been present a long time, with hypertrophy or contracture of the scalenus anterior muscle, scaleniotomy is indicated.

Treatment of Cerebral Palsies.—Phelps [18] stresses the complicated nature of the treatment required for cerebral palsy. The program must start in infancy and be correlated by the pediatrician, the orthopedist, the neurologist and the physical therapist. Educational and often

16. Ochsner, A.; Gage, M., and DeBakey, M.: Am. J. Surg. **28**:669, 1935.
17. Freiberg, J. A.: J. Bone & Joint Surg. **20**:860, 1938.
18. Phelps, W. M.: Care and Treatment of Cerebral Palsies, J. A. M. A. **111**: 1 (July 2) 1938.

psychologic aid are also needed. The general plan is to start in the primary stages with physical therapy and then to graduate into occupational therapy and finally into vocational training. Surgical intervention (when necessary) is considered only a step in the general treatment and is never curative in itself.

CIRCULATORY DISTURBANCES OF THE EXTREMITIES

Erythermalgia.—Smith and Allen [19] report the cases of 5 patients suffering from erythermalgia. They consider this a better name than the one given to the condition by S. Weir Mitchell, erythromelalgia. There is increased sensitiveness of the skin to rise in temperature above a certain point. The skin becomes red, hot and painful. One or more extremities may be involved. The condition may be primary, or it may be secondary to polycythemia. At present the treatment of choice is uncertain. A rise in cutaneous temperature above the critical point should be avoided if possible. Desensitization with baths of gradually increasing temperature may be tried. Roentgen therapy may sometimes be helpful.

Intermittent Vascular Occlusion in Peripheral Vascular Disease.—Collins and his co-workers [20] state that improved circulation in peripheral vascular disease is dependent on release of vasospasm and improvement of the collateral circulation. They report on 137 cases in which a pneumatic cuff was used about the thigh to produce intermittent venous compression. In the presence of open lesions, pressures of 30 to 40 mm. of mercury were used. When no lesions were present, pressures of 60 to 80 mm. were used. There were alternate periods of compression for one minute and release of compression for two minutes. There was prompt relief of pain in most instances, with healing of the ulcers in over 60 per cent. The diseases for which this treatment was tried included thromboangiitis, arteriosclerosis (diabetic and senile) and acute thromboses.

Peripheral Arterial Disease.—Samuels [21] divides peripheral arterial disease into two types: (1) organic disease and (2) vasomotor imbalance. He feels that palpation of the vessels of the foot is not a good way to determine circulatory efficiency. He has found the best clinical procedure to be that of watching the pallor of the sole of the foot with the leg raised 45 degrees from the supine position. While this is being done the patient rapidly flexes and extends the ankle. Differences

19. Smith, L. A., and Allen, E. V.: Am. Heart J. **16**:175, 1938.

20. Collins, W. S.; Wilensky, N. D., and Ginsberg, H.: Arch. Phys. Therapy **19**:261, 1938.

21. Samuels, S. S.: J. M. Soc. New Jersey **35**:224, 1938.

in cutaneous temperature, atrophy of the muscles of the calf and vascular calcification as observed roentgenographically are also useful criteria. In the presence of disease, smoking should be forbidden, and the natural heat of the extremity should be preserved with warm clothing. Hot baths and diathermy may be used to warm the limbs. Local means of applying heat should not be used, e. g., hot water bottles, which frequently cause burns. Intravenous injection of 300 cc. of a 2 per cent solution of sodium chloride every other day is helpful. This should not be used if there is nephritis or myocarditis. Exercises for the limb may be given if there are no lesions. The use of suction and pressure apparatus has not given particularly good results in organic lesions.

FOOT

Form of Foot of Mountain Nomads.—Frinak [22] made a study of the feet of the mountain nomads of Anatolia, who clamber over rocks continually. For shoes they wear a piece of hide tied on with thongs. The author examined 40 males and found them to possess uniform and characteristic feet. The form of the foot is grossly normal in that there is no flat foot and no valgus at the ankle. The foot is extraordinarily broad, measuring 11 to 13 cm. at the base of the toes. This width diminishes at the middle of the foot to 6 or 8 cm. The great toe uniformly deviates laterally from 12 to 16 degrees. The musculature of the toes and feet is unusually well developed. The great toe can be flexed 40 degrees dorsally and 70 degrees plantarward.

Roentgen Treatment of Plantar Warts.—Popp and Olds [23] report the results of roentgen treatment in 91 cases of plantar warts. In this series, 58 patients, or 63 per cent, were cured, whereas 18 patients, or 19 per cent, received no benefit whatever. In 40 of the 58 cured patients the lesion or lesions disappeared after one treatment; 11 required two treatments; 5 required three, and 2 were cured after four treatments. Thirty-two patients reported increased tenderness of the lesion in from seven to ten days after treatment. The average interval between the beginning of treatment and the disappearance of the lesions was six weeks.

[EDITORIAL NOTE.—Apparently several types of plantar warts are found. Some disappear spontaneously; others recede when undue pressure on certain areas of the foot is relieved by proper shoes or supports. Still others seem to be associated with epidermomycoses and to disappear with treatment of the fungus infection. Roentgen therapy is an effective treatment for many of them.]

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22. Frinak, S.: Ztschr. f. Orthop. **67**:396, 1938.
23. Popp, W. C., and Olds, J. W.: Radiology **31**:218, 1938.

OSSEOUS TUMORS

Giant Cell Tumor of Bone.—Coley and Higinbotham [24] state that the cause of this tumor remains unknown but that the traumatic theory offers the most logical explanation. The giant cell tumor of bone is found most frequently at the distal end of the femur and at the proximal end of the tibia, near the epiphysial line. The radius, humerus, ulna and fibula, in the order named, are the next most frequent locations. The giant cell tumor is usually benign, but occasionally it is encountered in a malignant form and this may represent a transformation of a tumor which was histologically benign at the onset. Treatment rarely consists in amputation. Surgical extirpation is preferable for accessible tumors and irradiation for inaccessible or extremely advanced growths. Caution should be exercised in using the roentgen ray, and histologic confirmation of the diagnosis should be secured in cases in which there may be an osteolytic sarcoma, which bears a close resemblance roentgenologically to the giant cell tumor. Irradiation should not be used in conjunction with surgical treatment; either the surgical method should bear the full responsibility or irradiation should. One must remember that the roentgen ray in large doses destroys the regenerative powers of bone. In small doses it may fail to arrest the disease; therefore, the exact dosage for the individual case is still a matter which no one understands. Still, inexpert irradiation is probably less hazardous than operation in the hands of one not familiar with surgical operative details, though loss of limb may ultimately result in either instance. If one resorts to operation, removal of all the tumor tissue through adequate exposure, careful closure of the wound without packing or drainage and primary healing of the wound should be sought. Of course, when surgical extirpation results in a weakening of the bony structure, protection during the regenerative phase is essential, for a pathologic fracture may cause functional impairment, and a painful condition of the neighboring joint may result.

Dawson and his associates [25] conclude that giant cell tumor of bone is a neoplastic growth probably originating with trauma and hemorrhage and developing as an osteogenic tissue reaction and proliferation which may slowly progress and ultimately regress but which in rare cases assumes the characteristics of an osteogenic sarcoma. It may be classed as a type of new growth intermediate between purely reactive tissue and true blastoma. Appended are 45 excellent photomicrographs of the types of tissue reaction met with, accompanied in each case by exceptionally lucid histologic and clinical notes.

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24. Coley, B. M., and Higinbotham, N. L.: J. Bone & Joint Surg. **20**:870, 1938.
25. Dawson, E. K.; Innes, J. R. M., and Harvey, W. F.: Edinburgh M. J. **45**: 491, 1938.

Primary Hemangioma Involving Bones of the Extremities.—Primary hemangioma of bone is a relatively uncommon tumor. Although Topfer [26] collected 257 cases of nonsymptomatic primary hemangioma of bone during 2,154 autopsies, in only 3 instances were the lesions in the extremities. The vertebrae were involved in all cases, and there were 34 instances of multiple lesions. Geschickter and Maseritz [27] were able to find reported in the literature only 11 cases of symptomatic primary hemangioma involving bones of the extremities, and they have added 4 more cases. The ages of the patients varied between 8 and 20 years. The distribution in regard to sex was equal. Three of the 4 patients gave a history of trauma. The roentgenologic changes characteristic of primary hemangioma of bone in an extremity are similar to those associated with benign giant cell tumor or osteitis fibrosa cystica, but there may be several significant features. First, the lesion tends to progress and may be more extensive than the other lesions under consideration commonly are. Second, the locules, when present, are smaller than the locules of benign giant cell tumor or benign bone cyst and are bordered by a much heavier framework of osseous tissue. Primary hemangioma of bone gives rise to cystic cavities which contain no capsular lining. Like bone cysts, they may contain fluid or tumor tissue within the wall. The tumor tissue filling these cavities is apparently similar to the tissue of angiomatous tumors elsewhere. The microscopic characters are various, and in the author's series there were a capillary hemangioma, cavernous hemangioma, an angioblastma and an angiosarcoma. A section of the capillary hemangioma showed areas of hemorrhage between which could be seen capillaries with their single layers of endothelium and a hyalin content. The tissues contained large cystic cavernous spaces filled with red blood cells and an occasional lymphocyte or polymorphonuclear leukocyte. Thus far the most valuable method of treating primary hemangioma of bone has been irradiation. Complete cures have been reported in a number of instances. The value of curettement is questionable. Resection of bone has been reported in several cases and has proved to be a means of absolute cure. The angioblastoma of bone in the case reported is the first to be described in the literature.

Myositis Ossificans.—Clinical and pathologic data on 25 cases of myositis ossificans, including both the circumscribed and the progressive form, are reviewed by Geschickter and Maseritz.[28] The circumscribed form is divided into only two clinical varieties, traumatic and nontraumatic. Fifteen of the patients, or 60 per cent, gave a history of

26. Topfer, D.: Frankfurt. Ztschr. f. Path. **36**:337, 1938.

27. Geschickter, C. F., and Maseritz, I. H.: J. Bone & Joint Surg. **20**: 888, 1938.

28. Geschickter, C. F., and Maseritz, I. H.: J. Bone & Joint Surg. **20**:661, 1938.

injury preceding muscular ossification. One case was noted in which there was fracture but no dislocation. The thigh was involved in 14 instances, the arm in 3, the elbow in 2 and the cervical and lumbar muscles in 1 instance each. The age of onset varied from 13 to 72 years. Sex appeared to be an outstanding factor: 23 patients were males. Two patients had myositis ossificans progressiva. Here trauma played an important role, but the etiologic agent is unknown. Both patients were females. The earliest physical finding is a viscid mass which gradually becomes indurated. It may make its appearance within a few hours. Roentgenograms at first show small discrete dense shadows which lie some distance from the normal bone. These areas gradually become confluent and form one large spicule of bone. The earliest roentgenographic appearance was nineteen days. The so-called dotted veil appearance has been called pathognomonic. When exposed at operation, the bone lesion is usually surrounded by a cartilaginous substance which appears to be the result of degeneration of muscle. Beneath this material a fibrous capsule is found. Radiating from the capsule are irregularly distributed bands of connective tissue which invade the bone. Occasionally cystic changes are found. The earliest histologic manifestations are degeneration of muscle, hyperplasia of connective tissue and organization of hemorrhage. There appears to be a tendency toward capsule formation, which is almost simultaneous with calcification of the inner portion of young connective tissue. Aggregations of colloid-like particles and bits of cartilage appear in some cases. Cartilage was distinguished in one fourth of the authors' cases. There was a single instance of malignant tumor complicating traumatic myositis ossificans. Conservative treatment is preferable. Postoperative recurrences are common in cases in which surgical removal is attempted before the condition has been present for six months or in which resection is not complete. Roentgen treatment is being tried; the results cannot be determined yet. Ossification occasionally regresses.

Osseous System in Hodgkin's Disease.—Abrams [29] made a study of 10 consecutive cases of Hodgkin's disease referred to the Brooklyn Cancer Institute. Two of the patients were found to be suffering from closely related diseases, lymphoepithelioma and lymphosarcoma. Of the remaining 8 patients, 6 showed involvement of the osseous system. The lesions are commonly multiple and may be osteoplastic, osteoclastic or both. The osseous lesions are usually demonstrated late in the course of the disease. Pain is commonly the first sign of osseous involvement. Roentgen therapy is palliative and retards the progress of the disease.

Skeletal Metastases in Cancer of the Breast.—There are three principal types of osseous localization for metastases from carcinoma of the

29. Abrams, H. S.: Ann. Surg. **108**:296, 1936.

breast.[30] Every large extension to the skeleton begins with a vertebral lesion, which extends later to the shoulder girdle and still later to the pelvic girdle. Finally, the entire skeleton may be involved if the patient survives. Involvement of a large part of the spine is more common than involvement of a single vertebra. There are three types of metastasis: (1) the osteolytic type, characterized by destruction and dissolution of bone; (2) the osteoplastic type, forming dense bone, and (3) the mixed type resembling Paget's disease, showing an osteolytic area surrounded by thickened cortex and sometimes presenting a mottled appearance. In general there are three distinct syndromes caused by metastases to bone from tumors of the breast: 1. The vertebral syndrome, or pseudo Pott's syndrome. The patient complains of pain in the spine, usually persistent day and night and not relieved by rest or immobilization. The symptoms tend to progress, fracture may occur, and compression of the spinal cord may result. 2. The scapulohumeral syndrome. The patient complains of pain in the shoulder, particularly in the region of the upper part of the humerus. Mild radiation of pain may occur but it is not like that of root pain. There is localized tenderness over the clavicle, the scapula or the humerus, with muscle spasm and weakness. The symptoms progress gradually and may result in a fracture, most commonly through the surgical neck of the humerus. 3. The pelvitrochanteric syndrome. The patient complains of pain in the hips, the pain being located in the region of the ilium, the pubis, the ischium or the greater trochanter. There may be vague radiation down the femoral or sciatic nerves. Spontaneous fractures through the upper part of the femur or in the pelvis may result. Any of these syndromes may progress until the metastases are spread diffusely throughout the skeleton.

Diagnosis of Hyperparathyroidism.—Garloch [31] discusses hyperparathyroidism and particularly the danger of confusing it with polyostotic fibrous dysplasia. A case illustrating this point is discussed in detail. The conclusions drawn are that a too hasty diagnosis of hyperthyroidism should not be made even when the values for calcium and phosphorus are outside normal limits and there is a negative calcium balance. If doubt exists as to the diagnosis a biopsy should be done of material from one of the cystic areas of bone. Pathologic examination will differentiate the two conditions.

KNEE

Cyst of the Internal Meniscus of the Knee.—Marchand and Guibert [32] state that cysts of the internal cartilage are much less frequent

30. Ducuing, J.: Presse méd. **46**:1225, 1938.
31. Garloch, J. H.: Ann. Surg. **108**: 347, 1938.
32. Marchand, L., and Guibert, H. L.: Ann. d'anat. path. **4**:389, 1938.

than cysts of the external cartilage. The internal cartilage is more firmly attached and is therefore more apt to tear from an injury, while the external cartilage, being loosely attached, is subjected to small traumas more productive of cyst formation. The pseudocystic degeneration usually involves the middle layer of the cartilage, and the inside of the cystic cavities has no endothelial lining. True cysts with endothelial lining are rare. The explanation of these cysts is uncertain. Some authors attribute them to embryonic inclusion of endothelial tissues in the cartilage during development, while others believe the cystic degeneration is due to trauma. A careful pathologic examination of a cyst of the internal cartilage is presented. There is an external layer of highly vascular connective tissue. The middle layer represents the external layers of the cartilage. The third is a fibrocartilaginous internal layer which is nothing but the less vascular middle zone and a portion of the avascular internal zone of the cartilage. These different zones present dissolutions of continuity of variable extent, which produce the pseudocystic effect. The formation of the pseudocyst is brought about by a swelling of the fibroblasts, the cytoplasm of which undergoes vacuolar degeneration. The enlarged cells then burst, and a cavity results, filled with a mucoid substance.

Demonstration of Articular Cartilage.—Nordheim [33] was able to demonstrate articular cartilage, particularly that of the knee, in roentgenograms by obtaining a partial vacuum in the joint by traction, abduction or adduction. He was able to demonstrate the medial meniscus in about 70 per cent of normal persons; the lateral meniscus could be demonstrated only rarely. If fluid was present in the knee it was impossible to show the meniscuses. A small amount of air injected into the joint aided in visualization of the cartilage.

33. Nordheim, Y.: Fortschr. a. d. Geb. d. Röntgenstrahlen **57**:479, 1938.

(To Be Concluded)